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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful – the editor, alone, is responsible for their type, their tone and their tenor.

ONE HAZARDOUS DAY

THERE is need for strengthening the present Food and Drug Act. It is outdated and outmoded by modern practices in the fields which it essays to cover.

Many persons, and especially those who think that new legislation might hurt their none-too-decent enterprises, have bitterly opposed such strengthening of the Act.

The fact of the matter, however, is that there is quite as much need today for a revision, a modernizing of this Act—as there was, when during the reign of Roosevelt I, Dr. Harvey W. Wiley championed so successfully the rights of the ultimate consumer.

So that the picture might be made more clear let us delineate just one day, one hazardous day, in the dietary of a Philadelphian of the eighties, before the Food and Drugs Act became effective.

Here it is!—One of the so-called *Good Old Days!*

"Out of bed at five-thirty—and up here in Northern Liberties we still have use for oil lamps. So I light one that stands on the table of my bedside. Now, this may blow up anytime, for they tell me that the Oil Companies have to find some way of getting rid of the gasoline, so they simply mix it with the kerosene. It will mean a fortune to the person who discovers some good use for this dangerous gasoline.

I wash up in the china bowl—and despite the fact that I have had my window down all night to keep the cold out—yet the water in the basin is covered with thin ice. But a little brisk lathering and brisker scrubbing sets my blood cells caroming through my constitution—and I feel fit as a fiddle—only some of the free alkali from this home-made soap gets in my eye and burns like the very dickens. Some day some bright aleck will invent a floating soap, 99.9 per cent. pure—then it won't be so difficult to find it under the bubbles. I needn't shave today—I have three days to go before the week's up. Oh, yes! tooth scrubbing—I must not forget that—still, I have to let it go, for I cannot find the sandstone. I guess Ma has taken it down-

stairs again to scrub the front door-steps. Well, I'm all set except my collar, and I'll have to wash that a bit. Now, let's see—I have to be careful to keep that away from the lamp—Sam Smith burned to death the other day when he lit a match on his celluloid shirt front.

Now for breakfast. Oatmeal and cream—the oatmeal tastes wormy, it probably is, and the cream is full of starch and fuller's earth. Still I eat, for *I know of no law to stop these things.* On comes the bacon and eggs—the bacon is all right, providing it survives the frying pan, because it has so much saltpeter in it, once a spark gets on it will burn to the bitter end—*and there's no law to stop it.* If the eggs were wine they'd be mellow and fit for a king—but eggs, unlike wine, do not improve with age. Anyway, Ma said the third one she opened was tolerably odorless. With breakfast there is at least one consolation, and that is, you cannot tell alum in toast bread. Ordinarily our bread tastes like a styptic pencil, but when toasted it is every bit as fine as motzas. Only the butter tastes queerly—some people call it pig butter, it has so much lard in it. Even the sea salt has sand in it—*and there's no law to stop it.*

Well, this cold weather, I always take my tonic after breakfast—essence of cod liver oil. They do say this cod liver oil is fine, and believe me, when I take a wineglass after breakfast I'm a new man. I feel tip-top, or shall I say tipsy-topsy. I never knew cod liver oil to be so tasty and to have so much authority. Pa says it has alcohol in it—I don't believe it—it doesn't say so on the label. If it did, I'd have to quit using it, because I'm the cheer leader in the Epworth League. Besides our deacon takes Peruna—and *there is no law to stop it.*

Now it's lunchtime—sausage and hot cakes. Fine! only there is no assurance that the meat is what it should be—a pig in a poke—anyway when fried it is rather hard to tell between pulverized pig and granulated goat. But so many people have died of poisoning through eating bad sausage recently, that one must be very particular about the last syllable in the word. Still, there is an advantage in dying from poison in sausage. Doctors say the body takes much longer to decompose.

Doctors call such poisons ptomaines, and if I remember my Greek properly, the word very appropriately came from *Ptoma,* meaning a corpse. Iunchtime I usually drink plenty of water—today I had no need to. The milk and the maple syrup were watered enough. And *there is no law to stop it.*

So to supper at six. Meantime I ate some candy, licorice lozenges, finished in two-tone lacquer. At least that is what a chemist told me about them. He said they were really poisonous—and that they were made of lampblack and glue with some sugar all melted together, molded into queer shapes and dipped in anise-flavored shellac varnish to make them keep. Well, I'm still alive—although something did give me a passing indigestion!

For supper we have a regular old-fashioned Philadelphia meal. Oysters to start—worried a little over that—for someone said typhoid comes from oysters brought up in beds that are not well aired. Then we had city-dressed beef (any city will do) and cabbage, potatoes, and green peas. Of course, one runs a risk these days with potatoes boiled in the jacket, there may be arsenic or paris green on them—and slug-shot in the cabbage. But the peas—Ireland was never so verdant! Every pea that rolled off Papa's steel knife left a trail of copper in its wake. Some things turn green with envy, peas turn green with copper sulphate. *Well, there's no law to stop it.*

Then, lastly, comes tea and baker's cake. The tea is fine, one needs to be very analytical to tell tea from dishwater, but the cake has yellow jaundice. Papa told the cook never to buy any more cake from that baker, because he buys his eggs from a chemical house. Nevertheless, I ate a lot of it, and thought it was fine, but how sick I got the next day.

First thing the doctor asked me was how long I had been a painter—and he wanted to diagnose my condition as painter's colic!

No wonder—I learned afterward that the bakers use chrome yellow (lead chromate) to color their angel cakes. It is much cheaper than eggs and much more colorful. Besides, it is a poison so appropriately used in angel cake—so mathematically correct—one cake equals one angel, etc. *And there's no law to stop it.*

So we come to the end of a more or less perfect day in the dietary of an old Philadelphian, and that our hero survived is only testimony to his Quaker sturdiness.

Still, I remind you, that even though the law protects our foods and medicines today, it does so most inadequately and we still exist in a world of hoaxes and hazards.

Hasten the day for the passage of legislation which will bring as much needed good to the present as the old Food and Drugs Act brought to its day and generation.

IVOR GRIFFITH.

ORIGINAL ARTICLES

THE PRINCIPAL CHEMICAL TESTS FOR MORPHINE

By Charles C. Fulton

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"The Author is, through wide experience, well qualified to write on this important subject. Actually this paper is a concentrate of a much more exhaustive presentation of his researches. The writer is the originator of many morphine tests, including seven of the principal tests, and some appear here for the first time in print. The article is not a compilation but an original classification, discussion, and evaluation of the best tests."

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R *Routine tests.*

The tests marked "R" are considered the 10 best for routine identification of seized morphine. They can all be made either on the spot-plate or the microscope slide, and all the necessary reagents, except Marquis', are entirely permanent.

T *Toxicologic tests.*

The tests marked "T" are considered the 10 best for the identification of small residues of extracted morphine. All are very sensitive and highly characteristic.

O *Opium tests.*

The tests marked "O" are applicable to an opium solution without isolation of the morphine. The three tests so marked above are reactions of certain true phenols, including morphine; most alkaloids do not interfere.

Discussion of Identification

MORPHINE cannot be identified with absolute certainty by any single test. The best crystal test, probably the one with Wagner's reagent, gives near certainty, but some other amine might give similar crystals. As for the best color test, no substance is known that will react at all like morphine with Reagent "C-2" except heroin or other closely related morphine derivatives; but the possibility remains that some phenol of very different derivation might give similar colors.

It is hardly necessary to say that for toxicologic tests the morphine must first be obtained as pure as possible.

Small amounts of oxidizing substances such as nitrates are capable of ruining the tests with concentrated sulfuric acid reagents, which are usually so valuable.

Phenolic compounds will interfere with the color tests, amines with the precipitation tests. Very small amounts of amine-impurities may prevent crystallization of the precipitates.

It is possible to identify morphine by color tests alone, or by crystal tests alone, but highly desirable that both kinds be used. When characteristic crystals can be obtained, they doubtless make the best tests. When color tests are mainly relied on, the proof of morphine is obviously improved if amine precipitation is also obtained, even if the precipitates refuse to crystallize.

Some of the tests suggested for routine (Nos. 7, 8, and in less measure 6 and 10) are rather general and are not recommended for any attempt to identify by a minimum number of tests. However, it takes only a few minutes to apply all ten tests recommended for routine, if the reagents are kept.

Usually three or four tests, properly selected, will make the identification absolutely certain, provided the exact morphine reactions are obtained.

ALKALOIDAL PRECIPITATION

Gelatinization Tests:

R 1. *Mayer's Reagent,* added to an aqueous solution on the spot plate, gives a whitish amorphous precipitate, quickly changing to a *pale yellow transparent jelly,* which can be poked out of the "spot" in lumps, with the finger, if the morphine solution was as concentrated as 1:500.

Under the microscope the precipitate, especially from dilute solutions down to about 1 :2000, shows characteristic rosette forms of indistinct structure. Definite crystals are also obtainable under certain conditions. The chief value of the reagent, however, is as a routine test for the spot plate.

This gelatinization test is specific; other alkaloids give precipitates with Mayer's reagent, but they do not gelatinize.

Reagent: A 2 per cent. KI solution saturated with HgI_2.

Morphine gives other gelatinous precipitates, notably with Marme's reagent (see test No. 3). The precipitate with Stannous H Iodide also, though it appears entirely crystalline under the microscope, is at least semi-gelatinous.

Micro-Crystal Tests:

R-T 2. *Wagner's Reagent,* with an aqueous (or concentrated HCl) solution of morphine, gives a heavy red-brown amorphous precipitate from which characteristic plate or *"parrot-feather" crystals* form. They are red, red-brown, or red-black, sometimes jagged square-cut plates, and sometimes feathered crystals or branching forms, often intermediate, or both types. An acid test drop aids the crystallization greatly. The best crystals are obtained from a solution about 1 :200 concentration; the usual sensitivity is about 1 :3000, but by special modification this can be increased to 1 :10000. The test is especially well known, and has been often described; photograph (1).

Crystals are given by many other alkaloids and amines, but in no case known do they look just like those of morphine, and in general they differ greatly, often in both form and color. This is probably the best crystal test for morphine. Formulas for the reagent differ somewhat. Wagner's No. 3 is recommended: Iodine—1 gm., KI—2¾ gm., Water—100 cc. Dissolve the I and KI in a little of the water, then add the rest. Stephenson used KI—5 gm., and this also gives good results.

R 3. *Marme's Reagent,* added to an aqueous solution of 1 :200 to 1 :1000 concentration, more or less promptly gives *long white needles, mostly grouped in sheaves,* without any amorphous precipitate. In more concentrated solution there is first a white amorphous precipitate which at once changes to a transparent

whitish jelly, in which or at the edge of which fine needle crystals can be seen (under the microscope) in great numbers. Considered by Stephenson the best test, it is indeed excellent for routine work. Photograph (1).

No other substance is known giving the same result as morphine.

The reagent: CdI_2—5 gm., KI 4.5 gm., Water—100 cc. (A more concentrated form is generally used, but this is unnecessary.)

4. *Stannous H Bromide,* added to an aqueous solution, gives a precipitate which crystallizes completely with great readiness, in very characteristic crystals: *Colorless grains bunched together in rosette forms* or *branching out from one another in fern-like forms.* Sensitive to 1:400.

The reagent: To 4.5 gm. NaBr in a test tube add 10 cc. $SnCl_2$ solution (3 gm. tin dissolved in 25 cc. concentrated HCl, 75 cc. water and a piece of tin added). Shake to dissolve the NaBr; preserve the Stannous condition with a piece of tin.

The reagent can be kept a month or so, but will not last indefinitely, and this together with the lack of any great sensitivity in the test, prevents it being as valuable as would otherwise be the case, considering the ease of crystal formation and the characteristic appearance of the crystals.

Stannous H Iodide (2) also crystallizes readily, giving small yellow spheres or rosette-aggregate of grains; sensitive to 1:800. However, this test seems not to be as satisfactory with the usual illicit morphine hydrochloride as with perfectly pure morphine solutions.

5. *Gold Bromide in Concentrated HCl,* applied directly to a little solid morphine or its salt, or added to a solution of morphine in concentrated HCl, after some time gives characteristic crystals, rosettes of *blades,* rosettes of *irregular plates,* or scattered *feathered plates, brownish-yellow or orange, red* where they overlap. Crystal formation usually requires about 10 or 15 minutes, with minute amounts even up to 2 hours. The crystals are largest and most beautiful at about 1:200 concentration, good ones are

obtained in half an hour with 1 :3000, a few small ones in 2 hours with a 1 :8000 solution, or by adding the reagent directly to a minute dry residue of as little as 0.004 mg. morphine.

This reagent gives different kinds of crystals with numerous alkaloids. The crystals of scopolamine resemble those of morphine, but are formed promptly.

The reagent for application directly to a solid alkaloid is:

Gold chloride crystals	1.5 gm.
NaBr	1.5 gm.
Concentrated HCl	90 cc.
Syrupy H_3PO_4	10 cc.

The phosphoric acid prevents the drop drying up, in testing for minute quantities by allowing it to stand a long time.

Gold Bromide in Concentrated HCl may also be added to an aqueous solution of morphine, the crystals then form on standing as *wavy branching threads,* often in rosettes. Crystallization is best with a 1 :400 solution; the ordinary sensitivity is about 1 :3000.

The reagent for addition to aqueous or concentrated HCl solution is:

Gold chloride crystals	5 gm.
NaBr	5 gm.
Concentrated HCl	100 cc.

This reagent, and the Stannous H Bromide reagent, have but recently been introduced by the writer.

Other Micro-Crystal Tests

Reinecke's salt, in freshly made, approximately saturated solution, gives rosettes of straggly threads or transparent plates, the color of the solution, sensitive to 1 :6000. The reagent will not keep.

Concentrated Dragendorff's Reagent gives small rosettes of needles and fuzzy rosette-bunches of tangled threads, later very small orange grains; sensitive to 1 :6000. The reagent will not keep indefinitely.

PHENOLIC COLOR TESTS

On the Aqueous Solution;

R 6. *Ferric Chloride.* The addition of a little $FeCl_3$ to a fairly strong neutral solution of a morphine salt gives a pure *blue* color. With the reagent in excess a blue-green or green is produced. The color will not appear in decidedly acid solution, nor in alcohol. The test is characteristic, but not very sensitive. A greenish color can be obtained with a 1 :500 solution, but a 1 :50 or stronger solution should be used if possible. A greater sensitivity can be attained by applying $FeCl_3$ solution, dilute or in very small amount, to solid morphine, but at its best the test cannot be recommended for sensitivity. This test is of course due to the phenolic character of morphine, and there are other phenols that yield blue and green colors, though not a great many. This is one of the oldest and best known tests, and the one which (in addition to solubilities) first showed that morphine is a phenol.

R-O 7. *Lefort Test.* To a morphine solution on the spot-plate add a drop or two of 5 per cent. iodic acid solution. A brownish-yellow color is produced. Add 2 or 3 drops of 10 per cent. NH_4OH and a *dark mahogany brown* color soon develops.

This test is very characteristic. With numerous reducing agents which might produce the yellow color, merely by freeing iodine, the addition of ammonia would decolorize the solution instead of darkening it. With morphine about half the yellow color is due to iodine set free; if this is extracted by chloroform or carbon disulfide the aqueous layer turns brown just the same on adding ammonia. The test is sensitive, as a 1 :7500 solution gives a yellowish-brownish color, a 1 :3000 solution a very distinct brown. It is not specific for morphine, being given by various phenols. Some further discussion follows the next test, which is closely related.

R-O 8. *Oxidation-Peroxide Test* (3). To morphine solution on the spot-plate add a drop or two of 5 per cent. HIO_3 solution, and 2 or 3 drops of ordinary 3 per cent. hydrogen peroxide. (Either may be added first.) A yellow color is produced with the HIO_3. Add 2 or 3 drops of 10 per cent. NH_4OH. A *pink* to *bright red* color is produced at once; slight pink with a 1 :7500

morphine solution, fairly strong pink with 1 :1000, red with 1 :500 or stronger. As in the preceding test, extraction of the iodine set free, before adding the ammonia, does not affect the test. The red color is not soluble in any immiscible solvent, so far as has been discovered.

This test is given by various phenols.

The two preceding tests are often useful as test tube reactions. They may be used in testing opium solutions. Even though the solutions are already brown, the change in one tube to a red color and in the other to a darker brown make very effective tests. Alcoholic solutions may be used. These tests can be obtained on morphine by using other oxidizing agents, but iodic acid seems to be by far the best thus far discovered. Fleury's test uses PbO_2, and bromine water has also been used.

9. *Copper Test.* To morphine solution on the spot-plate add 2 or 3 drops of 3 per cent. hydrogen peroxide, a drop or two of 10 per cent. ammonia, and stir with a copper wire, or a penny. A *pink* to *red* color is produced, the test succeeding easily with a 1 :3000 solution. Whether or not morphine is present there should be a conspicuous evolution of gas during the stirring; if not, the peroxide is too weak. In the absence of any reactive compound, the solution gradually dissolves copper and becomes blue. An alcoholic solution can be used. An excellent test, but one common to various phenols and their acetyl derivatives. (4). Heroin gives it as readily as morphine. This test is due originally to Denige's; Oliver introduced the method of stirring with a piece of copper.

Other Phenolic Color Tests on the Aqueous Solution

Radulescu's, or the Nitrous acid test, and the Diazo test may be mentioned. The latter was adapted to morphine by Lautenschlaeger, but is simply the long-known reaction by which an azo-dye is formed by the reaction of a diazonium salt with a phenol.

Phenols in general react in both these tests, some like morphine.

NITRATION

R 10. *Nitric Acid.* Concentrated nitric acid added to solid morphine or its salt gives strong *red* or *orange-red,* soon fading through orange to yellow. The red color is somewhat stronger with the common salts of morphine than with the free alkaloid. A red-orange can be noticed when the acid is added with as little as 0.05 mg., but the final yellow, or even a distinct orange on solution, requires much more morphine.

The test has little value for small brownish residues of extracted morphine, but as a routine test on seized morphine it is very useful. It is the test commonly relied on by the narcotic agents for a tentative identification. It is perhaps the only good color reaction in which codeine resembles morphine more closely than heroin does. (Codeine crystals turn orange and dissolve yellow; heroin gives pale yellow gradually becoming bright green). Pseudomorphine, orthodiphenol-oxymorphine, and probably some other oxidation products of morphine give the same reaction as morphine itself.

Brucine is the only substance commonly mentioned in the texts as likely to be mistaken for morphine in this test. It gives a much stronger red, which fades more slowly; but in small quantity or when mixed with an inert substance might be mistaken for morphine.

Various phenols, including pyrocatechin, vanillyl alcohol, arbutin and adrenalin come nearer to the morphine reaction; the last two have been submitted as samples suspected of being morphine. The majority of phenolic compounds give yellow or brown colors.

The addition of stannous chloride, after obtaining the nitric-acid reaction, is often recommended. Brucine then gives a violet color. The absence of this reaction, however, supplies exceedingly little confirmation of the presence of morphine.

When several different tests are made on the same spot-plate the Nitric acid test should not be made first, as the fumes will affect the morphine in the other "spots," modifying some of the reactions—the Marquis reaction, for instance, (No. 14) toward the reaction of test No. 16.

SULPHURIC ACID REAGENTS

Oxidizing Reagents

R-T 11. *Froehde's Reagent.* Molybdate in concentrated sulfuric acid. Added to a little morphine on the spot plate this produces an intense bright *purplish-red* color, after a little time (about four minutes), fading and passing through a comparatively weak brown or brownish, or with a very small quantity of morphine even fading out completely, then developing a strong bright *green.* On the spot plate this color ordinarily changes on standing to an olivaceous yellow-brown or brown yellow. This is due to absorption of moisture from the air. With several cc. in a test-tube the green solution, within about two hours, becomes a pure deep blue. Or, if the reaction is developed by heat, setting the spot plate on the boiling water bath immediately after adding the reagent, the purplish red color fades and passes quickly into the green, and with further heating is changed to *slate-blue.*

The hydrochloride of morphine gives first a *violet* color, accompanying the effervescence of HCl; but this quickly changes to the same purplish-red given by the sulfate. The color then passes through a weak brown to an *olivaceous green,* which persists as an olive-green, even if the solution is protected from absorbing water from the air, long after the sulfate solution has turned blue.

A single drop of the reagent, applied to a small dry deposit of morphine, shows the purplish-red, quickly fading, with 0.001 mg. In a dry atmosphere the green will develop with no more than 0.003 mg. The colors are quite plain throughout a "spot" full of reagent, with no more than 0.02 mg.

Phenolic compounds in general react, giving all kinds of colors and successions of colors. Some show resemblance to morphine in some degree, but it is not likely any of them would be mistaken for morphine.

The reagent is 0.5 gram sodium or ammonium molybdate dissolved in 100 cc. concentrated sulfuric acid with the aid of a little heat. It is permanent when kept in a glass-stoppered bottle.

Buckingham's reagent is 10 to 15 grams molybdate in 100 cc. H_2SO_4. It gives a stronger and more lasting initial *purplish-red* color, quite plain with 0.0004 mg. morphine. However, it does not give the fine green obtained with Froehde's reagent, and

finally the whole solution becomes a deep blue, which is primarily due to the reagent itself.

R-T 12. *Mecke's Reagent.* Selenious acid in concentrated sulfuric acid. Strikes pure *blue,* changing to a stronger *bluish green;* this changes slowly to olive-green, and finally to brown. With several cc. in a test tube the color, in about two hours, becomes red or brownish-red.

For certainty of obtaining the complete reaction in a "spot" full of reagent, about 0.05 mg. of morphine is necessary; for just an indication of morphine, using a single drop of reagent, 0.004 mg. will suffice to give a blue-green color.

With the hydrochloride of morphine the reagent strikes yellow, which at once passes through *olive-brown* to *green;* this changes to *greenish-blue* (or pure deep blue, in the test tube); slowly becoming dull bluish green. The initial colors are apt to appear confused and dirty. The U. S. P. X gives the erroneous impression that the reaction with the hydrochloride is the same as with the sulfate.

Unlike Froehde's reagent, Mecke's gives substantially as strong a reaction with codeine and dionine as with morphine; *green,* changing to *blue,* then slowly to green. Heroin reacts like morphine except that the reaction is less affected by the presence of chloride. Pseudomorphine gives a *violet* color, changing to brown, gradually to brown-orange; thus it is sharply distinguished from morphine by this reagent, both alkaloids giving strong reactions. Phenolic compounds in general react, giving various colors, but it is doubtful if any give the exact morphine reaction.

The reagent is made by dissolving 0.5 gram selenious acid in 100 cc. pure concentrated sulfuric acid. Solution takes place readily at room temperature.

13. *Flückiger's Reagent.* Titanic acid in concentrated sulfuric acid. This strikes with morphine a dull *purple* or *maroon* color, dissolving *maroon-red,* soon changing to plain *red,* gradually becoming scarlet. After the maroon-red the colors are likely to be rather dull or brownish.

Reagent: Digest 0.2 to 0.5 gram titanic acid anhydride in 100 cc. concentrated sulfuric acid for several hours at

140°-160° C. This will get it into solution, though it dissolves only with difficulty.

The strongest color is maroon-red. This appears with 0.001 mg. morphine, using 1 drop of reagent—the reaction has about the same sensitivity as Froehde's but the color does not appear as promptly. With a little more morphine the change to dull red is apparent. 0.01 mg. morphine will color a "spot" full of reagent a good maroon-red, 0.04 mg. will give the complete reaction.

Codeine and dionine give a somewhat similar, but comparatively very weak reaction.

With phenolic compounds in general, titanic acid is very reactive. The color most often produced is orange to scarlet-red, and a strong orange is produced with some compounds which give weak colors or none at all with other sulfuric acid reagents. Some phenols give maroon-red to purple colors, considerable resemblance to the morphine reaction being noted with thymol and 4-hydroxy-1-2-dimethyl-benzene; and some resemblance with others. Other colors (aside from brown) are exceptional.

ALDEHYDE REAGENTS

R-T 14. *Marquis' Reagent.* Formaldehyde in concentrated sulfuric acid. This gives, first, a strong *purplish-red* color, closely similar to the initial color with Froehde's reagent. This color soon changed to *red-purple,* gradually *purple;* finally, but rather slowly, becoming blue.

This is one of the best, most characteristic, and most sensitive tests for morphine. Even under adverse conditions (as a very humid day) and using a "spot" full of reagent, the complete reaction is obtained with 0.03 mg. morphine, and often 0.01 to 0.02 mg. will give the final blue, as well as the preceding colors. Using only 1 drop of reagent, 0.005 mg. shows the red-purple changing to purple quite plainly, and a purple color, but no definite succession of colors, is obtained with 0.002 mg.

With the hydrochloride the reagent strikes an orangish color, which instantly changed to intense crimson; this changes to purple and more slowly to blue, as with the sulfate.

The reagent consists of 1 to 3 drops of formaldehyde solution (37-40 per cent.) in 3 cc. concentrated H_2SO_4. The writer has followed Mulliken in considering 2 drops HCHO / 3 cc.

H_2SO_4 as the standard. (5) Apparently this reagent will not keep indefinitely, but for those who use it frequently, about 25 cc. made up in a small rubber bulb dropping flask will prove very convenient.

The formaldehyde reaction with morphine seems really best and strongest with acid about 6 plus 1, or 87 per cent. H_2SO_4. Comparing this form of the reagent with the standard Marquis', the sensitivity is the same, the purple color of maximum intensity develops more promptly and is a little brighter, but the change of colors in the course of the reaction does not cover so wide a range. A *purple-red* color is produced, changing to *purple* and gradually to deep *violet*.

The majority of phenolic compounds give red or brown colors. A few, including pyrocatechin, vanillyl alcohol, guaiacol, and veratrol give purple-red or purple, and might conceivably be confused with morphine or another opium alkaloid by this test alone.

15. *Wasicky's Reagent.* Para-dimethyl-amino-benzaldehyde in concentrated H_2SO_4. Strikes a strong *orange-red* to *scarlet*, dissolving to form an *orange* to *scarlet* solution. The color is similar to the orange-red with concentrated nitric acid (test No. 10).

This reagent is more sensitive even than Marquis' toward perfectly pure morphine. However, the color produced in testing traces (orange) is one that may be masked by a brownish color due to impurities. Under favorable conditions of purity the orange color is quite distinct with 0.001 mg. morphine, using 1 drop of reagent; and 0.01 mg. will color a "spot" full of reagent a good orange. There is no succession of colors.

Various phenols and phenolic compounds give strong yellow, orange or scarlet colors. Heroin, codeine and dionine give the same color as morphine; pseudomorphine gives no color at first, gradually a weak green.

The reagent has been recommended by a number of authors; according to Balls & Wolff it was first proposed by Wasicky. It was made in this study by dissolving 0.3 gram of the aldehyde in 10 cc. of 8½ plus 1½ sulfuric acid (about 87 per cent. H_2SO_4). The quantity of aldehyde and the strength of the acid can be varied quite a little from this formula without changing the reaction much.

Other Aldehyde Tests

Another aldehyde test is with furfural. It is not of much importance, but sometimes shows up as a pink or weak red color produced with morphine tablets by pure sulfuric acid, furfural being formed by the action of the acid from sugar present.

Hydrastine, when mixed with morphine, will act as an aldehyde when the mixture is treated with concentrated sulfuric acid.

ALDEHYDE OXIDATION REACTIONS

T 16. *Reagent "C-2."* Formaldehyde and ferric salt in concentrated sulfuric acid. Strikes *purple-red,* at once changing to *green* with flecks of *violet;* stirring as quickly as possible the solution is bright *green,* quickly changing to strong *dark blue;* after a little dull *purple-red,* becoming dull *dark red,* and finally greenish-brown.

A complete reaction can be obtained with 0.03 mg. morphine. Using 1 drop of reagent, 0.007 mg. showed purple-red changing to bluish green, then to blue; and a slight bluish-green color was obtained with 0.002 mg.

Phenols react, giving various colors, but no compound is known that could possibly be mistaken for morphine in this test.

The reagent: To 1 drop formaldehyde solution (40 per cent.) add 6 cc. concentrated H_2SO_4 and 0.2 cc. 10 per cent. ferric sulfate solution. Mix while cooling. Or, use 3 cc. concentrated H_2SO_4 and 1 cc. fuming H_2SO_4 (15 per cent. free SO_3) with the same amounts, 1 drop and 0.2 cc. respectively, of HCHO and $Fe_2(SO_4)_3$ solutions.

This is a modification of Reagent "C." (6) The morphine reaction is the same as with Reagent "A," the original reagent of this kind. (3)

There are a number of other aldehyde-oxidation reactions, but they are of less importance.

Lloyd's test, in which a mixture of morphine and hydrastine is treated with sulfuric acid and an oxidizing agent, with production of a color reaction, belongs to this group.

REAGENT TESTS

The reagent tests for morphine are reduction tests, the principal ones being:

(a) Iodic acid reduced to iodine; colors CS_2 or $CHCl_3$ purple.

(b) Ferric-ferricyanide reduced to Prussian blue; blue color or precipitate.

(c) Phosphomolybdic acid reduced; blue color with ammonia.

(d) Ammoniacal silver nitrate reduced to silver.

NEGATIVE TESTS

(a) No marked color with pure sulfuric acid at room temperature.

(b) No response in the brucine test, after treatment with HNO_3 (purple color on adding $SnCl_2$ or sodium thiosulfate solution).

(c) Not precipitated by alkali in excess.

DERIVATIVE TESTS

Besides the four types given below, there are also derivative tests based on conversion to pseudomorphine.(7)

Orthodiphenol-Oxymorphine

17. *Oxidation Orthodiphenol test.* To 2 to 5 cc. of morphine solution in a test tube add 1 or 2 drops of 5 per cent. HIO_3. Add a drop or two of 1 per cent. $Fe_2(SO_4)_3$ or other ferric salt, and divide the solution into two or three parts for the following reactions. (If desired, the iodine set free may be extracted with chloroform. This will not affect the oxymorphine in the aqueous layer.)

(1) To 1 to 2 cc. of solution add an excess of $NaHCO_3$. A *pink* to *deep red* color is produced. A 1:20,000 morphine solution yields a slight pink, a 1:5000 solution a good *purplish-pink*.

(2) To 1 to 2 cc. of solution add 1 drop of concentrated H_2SO_4, then as much ammonium acetate as will dissolve readily. A *blue* color is produced. A light blue-green can be obtained with a 1:10,000 morphine solution, a deep blue with 1:1000.

This reaction is one of the best morphine tests for an opium solution. Procedure (1) is very convenient and satisfactory. Procedure (2) generally yields a dark green. Dilution will often lessen interfering colors and improve the effect.

Apomorphine

T 18. *Pellagri's Test.* Dissolve a little morphine or its salt in a test tube in a few drops of 85 per cent. H_3PO_4 (syrupy), and heat to boiling for a moment. Cool and add 2 to 3 cc. water. Add a drop or two of 5 per cent. HIO_3 solution. An *orange* to *bright red* color is produced, the color of the oxidation product in decidedly acid solution. Add considerable sodium acetate or ammonium acetate and the color is soon changed to bright *green* or strong *blue-green.* Shake the solution thoroughly with ether and the latter extracts the color, becoming purplish-pink to strong *magenta red.* Amyl alcohol extracts a pure *blue,* ethyl acetate a *violet.* Organic solvents in general will extract the colored compound completely, or nearly so, becoming blue, violet, purple or red. However, when iodic acid is used to oxidize, an organic solvent containing oxygen must be used, lest the iodine set free itself impart a purple or violet color. To ether, amyl alcohol or ethyl acetate a little free iodine imparts merely a yellowish or brownish color. Pellagri's test is sensitive to about 0.03 mg. of morphine.

A good alternative oxidizing agent is $HgCl_2$. Form apomorphine as before, dilute the H_3PO_4 with 2 to 3 cc. of strong sodium acetate solution, and add a few drops of 5 per cent. $HgCl_2$. Heat in the boiling water bath, or boil the solution itself for a short time. Apomorphine, if present, is oxidized to the characteristic green compound. Organic solvents extract their characteristic colors. With this method chloroform, benzene, xylene, etc., can be used to extract the color if desired. This method of oxidation is due to Grimbert & Leclere.

The formation of apomorphine may also be used for an orthodiphenol test. For this purpose conversion by boiling in melted oxalic acid is better than by boiling in phosphoric acid.

Sulfomorphid, or Apomorphine-Sulfonic-Acid

A number of derivative tests can be based on conversion to this compound—formation of the crystalline compound, fluorescence test, orthodiphenol test, Husemann's test, etc.(3) The oxidation test given below is perhaps the best.

T 19. *Sulfomorphid Oxidation Test.* Put a little dry morphine or its salt in a dry test tube and dissolve in several drops of pure concentrated sulfuric acid. Stand the tube in a beaker of water warmed to 40° C., for 7 or 8 minutes. Remove the tube and add water, allowing about 1 cc. water for every 3 or 4 drops H_2SO_4 used. (If a larger volume is wanted, oxidize first, then dilute). Add a few drops of 5 per cent. HIO_3 solution, and an *orange* to *bright red* color is produced. Add considerable sodium acetate, and the color becomes *bright green* to *deep blue-green.* Shake with some amyl alcohol. The color, or at least a large part of it, is extracted by this organic solvent, which becomes *blue.* Ether and most other organic solvents will not extract this product at all; the color is soluble, besides its aqueous solution, only in the lower alcohols and in acetone, so far as has been discovered, and is blue in these solvents.

Ammonia test: To the *green* solution add an excess of concentrated NH_4OH equal to half the volume of the solution. The color becomes purplish-blue. From this solution amyl alcohol extracts the color, becoming a fine *purple.* Ammonia cannot usefully be employed to change the orange-red solution to green or blue.

If the sulfuric acid solution of the morphine is heated too long or too hot (80°-140°) oxidation by HIO_3 after dilution will still produce the same orange-red, changing to the same green on neutralizing the effective acid, but neither amyl alcohol nor any other immiscible organic solvent will extract the color.

The alternative method of oxidation described for Pellagri's test (Grimbert & Leclere's, heating the diluted solution with sodium acetate and a little $HgCl_2$) can also be used in this test.

The colors described for the aqueous solution and both the blue and the purple (ammonia test) in amyl alcohol can be obtained with 0.04 mg. morphine.

Oxidation Concurrent with Heating or Standing in Sulfuric Acid

T 20. *Bromide test.* Mix a little dry morphine or its salt in a test tube with a pinch of NaBr, and add 8 or 10 drops of concentrated H_2SO_4. Shake the tube a little to ensure contact of the acid with the morphine, then stand it in the boiling water bath for a few minutes. The color of the solution is then generally dark *green,* due to the morphine, but it may vary to red-brown, due to the bromide. At this point see that no morphine is floating undissolved on the acid. Dilution with ½ cc. water for each drop H_2SO_4 gives a solution with a strong bluish-green color, and a *dark green precipitate* soon forms. Amyl alcohol readily extracts deep *green,* benzene or ethyl acetate deep *blue* to *violet-blue.* Chloroform, on shaking well, becomes green, or with more morphine *blue-green* to deep *blue.* Ether, shaken with the solution which is still warm from the dilution, extracts a *violet* color, but as the solvent cools (which of course occurs quickly) it deposits a green sediment on the sides of the test tube, losing most of its color, and thus appearing to change to a weak gray.

In this test the bromide is decomposed by the hot sulfuric acid, and the morphine oxidized by the bromine set free. The test is not much affected by temperature. In the presence of an oxidizing agent, such as chromate or arsenate, which will free the bromine, it can be obtained easily at room temperature. When the tube is heated as described the spontaneous decomposition of the bromide is sufficient. Chloride gives a rather similar test when an oxidizing agent is present to free chlorine.

Codeine and dionine, as well as heroin, react like morphine. Thebaine, also, gives a similar test.

This test can be obtained with 0.02 mg. morphine and should be unmistakable with 0.04 mg.

T 21. *Arsenate test, 130° C.:*

(a) Colors in the H_2SO_4 solution.

In a test tube dissolve a little morphine (free alkaloid or sulfate) in about 8 drops concentrated H_2SO_4. Add 4

drops of concentrated H_2SO_4 containing 0.5 gram KH_2AsO_4 (or sodium arsenate) per 10 cc. (dissolved by heating on the water-bath). A weak blue color is produced at once, if a fairly large amount of freshly dissolved morphine is present; but this color is not to be depended on. Stand the tube in a suitable bath (glycerine, for instance), and heat. At about 30°-40° C. (or after standing some time at room temperature) a *green* color develops, and soon becomes strong *dark green.* At 60°-70° this begins to change to blue, and soon becomes *dark blue.* At about 115° it changes back to *dark green,* and this color, or green-black, will persist until about 200°, when charring makes the solution a dirty brown-black. For the further developments of the test, however, remove the tube at about 130° (allowable range 120°-145°). Cool.

(b) Colors in water and solvents.

Dilute the dark green solution with water. A little dilution (with 0.6 cc. water, or 0.1 cc. to 2 drops H_2SO_4) changes the color to *deep red;* with further dilution a *dark blue* solution results, in which a dark precipitate soon forms on standing. The final dilution ordinarily used is with 6 cc. water, or ½ cc. for each drop of H_2SO_4 used. Shake portions with solvents; amyl alcohol extracts deep *violet-blue,* chloroform *violet,* ether *magenta red,* benzene or ethyl acetate lavender to *purple.* Amyl alcohol is the best solvent of the five, but the others extract good colors.

Heroin reacts the same; codeine, dionine, and thebaine similarly.

Sensitive to 0.02 mg., if the quantities of reagents are reduced somewhat.

Different colors in the solvents can be obtained by heating to 175° instead of 130°.(8)

Perchlorate can be used instead of arsenate, for a rather similar test (8). Chromate reactions were also previously described, but are too uncertain to be practical, as over-oxidation occurs so frequently.

— Suggested Tests for the Routine Identification of Seized Morphine —

¢ is used as a symbol for "changes to" or "changing to"

H—Heroin C—Codeine D—Dionine

Reagent	Morphine Reaction	Reaction of Derivatives	Test
SPOT-PLATE TESTS ON THE SOLID SUBSTANCE			
(1) Froehde's	*purplish red* ¢ weaker brown ¢ green (hydrochloride—strikes violet)	H same C & D weak green ¢ blue	#11
(2) Mecke's	blue ¢ *bluish green* (hydrochloride—strikes yellow-olive, dissolves green ¢ greenish blue)	H same C & D similar, green ¢ blue ¢ green	#12
(3) Marquis'	*purplish red* ¢ *purple* ¢ blue (87% H_2SO_4 may be preferred to concentrated for this test)	H same C & D similar bluer color at start	#14
(4) HNO_3	*orange-red* ¢ orange ¢ yellow	C & D similar, but weaker; orange ¢ yellow. Pure H different, yellowish ¢ green	#10

	Spot-Plate Tests on the Aqueous Solution			
(5)	$FeCl_3$	blue (green with excess reagent)	C, D & H negative	#6
(6)	Mayer's	ppt., quickly becomes transparent yellowish jelly	C, D & H give ppts., not gelatinous	#1
(7)	HIO_3 & NH_4OH (Lefort test)	dark brown color	C & D negative H negative or very weak	#7
(8)	HIO_3, H_2O_2 & NH_4OH (Oxidation-peroxide test)	bright red color	C & D negative H negative or very weak	#8
	Tests for the Microscope Slide, Aqueous Solution			
(9)	Wagner's (acidify the test drop)	amorphous ppt., yielding red, red-brown, red-black plates & branching forms—"parrot's feather" crystals	H amorphous ppt. C & D yield crystals related to those of M; C crystals yellow to yellow-brown	#2
(10)	Marme's	gelatinous ppt., white needles in sheaves	H amorphous C & D different crystals	#3

REFERENCES

The writer has made no attempt to compile descriptions of the morphine tests as they are given by various authors. His whole purpose has been to describe them as observed in experiments and practical experience over a period of twelve years. Consequently, in the short list below, half the references are to his own published work:

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ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Bacteriology . . . . Louis Gershenfeld, B. Sc., Ph M.
Biochemistry, Nutrition, etc. . . . Arno Viehoever, Ph. D.
Biology . . . . . Marin S. Dunn, Ph. D.
Chemistry . . . . . Arthur Osol, Ph. D.
Pharmacy . . . . . E. Fullerton Cook, Ph. M.
and their assistants

The Staling of Coffee. S. C. Prescott, R. L. Emerson and L. V. Peakes, Jr. *Food Research 2,* 1 (1937). Although considerable work has been done on the subject of the chemistry of deterioration of coffee, the knowledge of the chemical changes responsible for loss or modification of flavor in freshly roasted coffee is far from complete. Accordingly the authors carried on a searching chemical investigation of coffee and various fractions isolated from it.

The results of the present investigation do not wholly agree with those of any previous investigation. The present workers do agree that furfuryl alcohol is the chief neutral constituent of the aromatic oils of coffee. They disagree with Erdmann, however, in finding that acetic acid is the principal acid of the volatile portion, the former having found a valeric acid to be the main component.

Prescott and associates found the mixture of volatile ingredients extracted from coffee to become darker and finally resinify upon standing. If exposed to air this change is very evident even overnight. Sealed in an evacuated tube the change is much retarded. In order to test whether this decomposition could have anything to do with the unpleasant taste of stale coffee, small portions of a freshly distilled and of a dark sample which had been exposed to air for some time following distillation were dissolved in equal amounts of water and tasted. The solution of the old sample left an unpleasant bitter taste in the mouth. This was entirely absent in the case of solution of the freshly distilled sample. Another test was run on a mixture of furfuryl alcohol and its acetic and formic esters. After eight weeks the sample in an unsealed tube had become quite brown, that in a sealed tube under an air pressure of two millimeters was a

very pale yellow, while that placed in an atmosphere having a 75 per cent. humidity was a dark brown. Only the sample kept in a moist atmosphere had gone off appreciably in taste. These results confirm the findings that coffee kept in a vacuum is the best preserved, that in air is not nearly so well preserved, and that in a moist atmosphere it deteriorates very fast. The authors conclude that the mixture of volatile ingredients would seem to be in part responsible for the staleness of coffee, but they would also point to the possibility of any other group of compounds other than the fat being responsible for staleness of coffee. A. O.

Sterols. VIII. Preparation of Androstanedione from Allo-Pregnandiol. R. E. Marker, O. Kamm, D. M. Jones and T. S. Oakwood. *J. Am. Chem Soc. 59,* 614 (1937). Under this title the authors describe experiments by means of which a complete structural relationship between the female sex hormone, progesterone, and the male sex hormone, androsterone, is established. Briefly, the relationship was derived by converting *allo*-pregnandiol, a reduction product of progesterone, to androstanedione, an oxidation product of androsterone.

Starting with a mixture of *allo*-pregnandiol and pregnandiol, progesterone reduction products obtained from concentrates of human pregnancy urine, the mixture was oxidized by chromic anhydride to *allo*-pregnandione which was purified by crystallization from acetone. The latter was reduced in acetic acid at room temperature with platinum oxide and hydrogen to *allo*-pregnandiol. The diol was converted to a diacetate. The acetyl group in the 3-position of this compound was replaced by a hydroxyl group by hydrolysis with potassium hydroxide in methyl alcohol solution at 15 degrees to 20 degrees C., and then converted to a keto group by oxidation with chromic anhydride. Hydrolysis of the other acetyl group, which occurs in 20-position, resulted in the compound *allo*-pregnanol-20-one-3. This compound was converted to androstanedione by a series of reactions involving dehydration with anhydrous zinc chloride in acetic acid, ozonization of the resulting compound and decomposition of the ozonide by heating with acetic acid. One of the two products obtained in this series of reactions was found to be androstanedione, identical in composition with the product obtained by oxidation of the male sex hormone androsterone. A. O.

Research on the Emulsification Power of Infusions of Medicinal Plants. L. I. Weber and L. Legoix. *J. Pharm. et Chemie 129,* 24 (1937). A series of experiments were made to see if the emulsion of oily substances in water was different from that obtained with plant infusions.

Method used: In a glass tube, tapered at the bottom and fitted there by a rubber tube which is closed by the aid of a clamp, add 1 cc. of oily substance and 10 cc. of a solution of 10 p. in 100, of an infusion. Then stopper it with a rubber stopper, agitate for three minutes and set it aside. After a time, allow 5 cc. of the mixture to flow, and examine the first drop (after this 5 cc. flow) under the microscope. Thus the examination is always carried out upon the middle stratum of the emulsion.

Emulsions of olive oil, castor oil, cedar oil, melted butter and cod liver oil have been examined.

The emulsions were set aside one and one-half hours and then examined. Those made with pure water contained a number of oil drops of different dimensions. Those made with infusions contain a greater number (two to four times more) of oil drops, generally of smaller dimensions.

The infusions studied for the emulsification of oily substances were of absinthe, mint, senna, centaury and saponaria. The first three gave greater (dimensions) oil droplets than the last two. The infusions of gentian, rosemary and thyme behave almost like the pure water.

Dyes were used to stain the oil drops in order to facilitate their observation, but it must be remarked that introduction of a new substance can change the system of emulsion.

In general the authors find that the infusions of plants favor the emulsion of oily substance, giving them more stability than water.

B. M.

The Significance of the Adrenals for Adaptation. Hans Selye. *Science 85,* 247 (1937). Symptoms of adrenal deficiency observed in the study of the alarm reaction are almost identical to those observed in non-adrenalectomized animals after exposure to serious damage. The conclusion is that there is no specific change characteristic of adrenal deficiency, and that the changes observed after removal of the adrenals are due to response of the organism to gen-

eral damage, i. e., they are caused by the alarm reaction. Alarming stimuli were found to cause more pronounced changes in the adrenalectomized animal than in the normal, suggesting that the function of the adrenals is to increase the resistance of the organism to alarming stimuli. In support of this, enlargement of the adrenals was observed in animals constantly exposed to damaging stimuli.

It is claimed that some functions of the adrenals are to maintain normal body temperature, prevent fatigue following muscular exercise, to detoxify harmful substances, and to maintain a constant blood sugar level. Decreased resistance to agents acting as alarming stimuli, such as variable temperature, muscular exercise and toxic drugs, is to be expected if we suppose that the function of the adrenals is to prevent damaging effects of the alarm reaction. Experiments with a large number of rats adapted to cold, muscular exercise, etc., show that even the adrenalectomized animals tolerate exposure to stimuli very well, while non-adapted adrenalectomized controls are killed.

From observations it is concluded that one of the most important functions of the adrenals is to increase the resistance to alarming stimuli. However, when first confronted with the stimuli, the adrenals of the organism play an important part in the first stage of adaptation to conditions of the environment. Changes necessary for further adaptation take place in the peripheral tissues. In this stage the stimulus ceases to be "alarming" and the adrenal hormones are no longer required for adaptation. E. H. MACL.

Soap Preservatives. Paul I. Smith. *Soap 12,* 4 (1937). Increased costs of fatty materials has caused the soap industry to resort to the use of lower grade raw materials with the increased risk of rancidity and discoloration in the finished product. This has caused greater attention to be given to the use of antioxidants and preservatives, which permit the use of these lower grade fats, oils and fatty acids and prevents a change in the finished stock. Uniformity of results makes it necessary for a manufacturer to use a preservative which is not attacked by salt, free alkali, antiseptics or perfumes. Sodium thiosulphate, one of the best known and most economical preservatives, is attacked by certain essential oils and some chemicals of an acidic nature, while sodium sulfite may cause discoloration or spottiness in a soap which contains iron or copper which have been introduced by the use of off-grade caustic, silicate, rosin or salt.

Several causes of rancidity are given, as follows: 1. Use of low-grade fats and off-grade chemicals. 2. Bad processing. 3. Corrosion in plant equipment. 4. Unsuitable storage and packaging methods. Perfumes are not considered to be the cause of rancidity by the author.

The ideal soap preservative is one which possesses the following qualities: 1. Will not change the color or perfume of the soap. 2. Will not cause brittleness in the soap. 3. Will not reduce the soap's lathering power. 4. Will not react with the fatty acids or alkalies. 5. Will be soluble in the fat or alkali. 6. Will be effective in small quantities. 7. Will not cost any more than the soap. The following list of preservatives was suggested several years ago: Borax, sodium thiosulfate, sodium hydrosulfite, sodium sulfite, salicylic acid, sodium salicylate, benzoic acid and sodium benzoate. To this list has been added stannous chloride, stannous oxide, sodium stannate, magnesium silicate and formalin paraformaldehyde. Limited use is also made of derivatives of polyhydric phenols containing hydroxyl groups together with ethyl ether, propenyl and ethyl groups. Soaps may also be hydrogenated, deodorized or bleached by means of nascent hydrogen produced during the saponification process by using zinc or aluminum. The author considers sodium hydrosulfite an excellent preservative and bleach particularly when dark colored oils are used. While sulfites, hydrosulfites and thiosulfates may cause discoloration in a soap by the action on the brass, copper or iron equipment of the plant, borax is found to be very resistant to metals but not so good a preservative as sulfite. H. P. F.

Agricultural Insecticides. R. B. Stoddard. *Soap 12,* 4 (1937). The need for more effective insecticides for use in the agricultural field together with the recognition by the government that the unrestricted use of poisonous materials on edible fruits and vegetables could no longer be permitted, has caused many changes in the commercial and technical phases of the insecticide industry.

The rapid multiplication of insect pests in the past decade or two is traced by the author to two causes—large scale cultivation of vegetables and fruits in concentrated areas, and the unintentional transportation of these insect pests into new areas where their multiplication is possible due to the absence of the natural enemies which had held them in check in their former habitat.

The heavy chemical industry has been largely responsible for the production of the well known insecticides of the copper, lead and arsenic type. The economical production of these substances was only possible due to the fact that the chemical industry possessed the necessary large capital investments, suitable equipment for volume production and extensive sales organizations.

With the agitation against poisonous residues and the quest for more efficient insecticides the limelight has been turned on the so-called botanical insecticide, and at present the interest is directed mainly on the rotenone bearing roots such as derris, cube and to a certain extent on pyrethrum. These products meet the present essential requirements of efficiency, safety, availability in quantities, and reasonable cost, but the extent to which they will displace the older type of insecticide or how soon a cheaper or more efficient product will be found remains still a conjecture.

The fact that the investment required on the part of the producer of the botanical insecticide is relatively small when compared with the investment required for the production of the insecticide of the heavy chemical type, has opened the field to new competition. Individual initiative, technical skill and some little capital has produced new products and developed new methods of using the botanical insecticides which has added materially to our knowledge of their present value and future potentialities. The author believes the possibilities of derris and cube have so far been only lightly touched, and better and more effective methods of using these products will open new fields. Pyrethrum, although better known, has certain limitations which may be overcome through future developments. The biological control of insect pests is considered to be of limited application and offers the danger that the cure may be worse than the disease. H. P. F.

The Isolation of Muscle Nuclei. G. Crossman. *Science 85,* 250 (1937). The following is a method for freeing nuclei from the cytoplasm of smooth, striated or cardiac muscle, yielding a permanently stained preparation for study. Nuclei for chemical analysis can also be obtained in this manner.

1. Smear slide with Mayer's egg albumen.
2. Place drop of 5 per cent. citric acid in center of slide.

3. Add small piece of fresh muscle. Infiltration renders the tissue translucent, and gentle teasing will aid the separation of the nuclei.

4. Remove muscle with forceps. The drop contains free nuclei.

5. Allow to almost dry. Place slide in 95 per cent. alcohol to coagulate.

6. Rinse in several changes of tap water, then distilled water.

7. Transfer to Mayer's hemalum to stain nuclei.

8. Wash in tap water until blue.

9. Counterstain in eosin.

10. Dehydrate, clear and mount.

The resulting preparation shows nuclei stained blue on a homogenous eosin background. Inferior results are obtained with other body tissues. E. H. MACL.

A Useful Fiber Stain for the Paper Chemist. W. H. Boast. *Chemist Analyst 26,* 30 (1937). The author reports the following staining method for the differentiation in the same field under the microscope of bleached sulfite fibers, unbleached sulfite fibers, bleached deciduous soda fibers, rag fibers and mechanical ground wood fibers found in white shavings in the top-liner furnish of white patent coated boards:

Three solutions are used. Solution A, N/10 $FeCl_3$ (2.7 g. of $FeCl_3.6H_2O$ in 100 cc. of distilled water). Solution B, N/10 $K_3Fe(CN)_6$ (3.29 g. of potassium ferricyanide in 100 cc. of distilled water). Solution C. Dissolve 100 g. of calcium nitrate in 50 cc. of distilled water. Add 3 cc. of a solution made by dissolving 8 g. of potassium iodide in 90 cc. of distilled water, and adding 1 g. of iodine, and allow to stand for a week before use.

Transfer the fibers of the defiberized sample of white shavings to a slide by the dropper method. Remove water by evaporation. Place the slide, for three minutes at 20 degrees C., in a mixture of 10 cc. of solution A, plus 10 cc. of solution B. Wash slide by dipping in distilled water three times. Dry slide by evaporation. Add three drops of solution C to the fibers and after one minute cover with cover glass and examine.

Bleached sulfite fibers become pink; unbleached sulfite fibers, blue; bleached deciduous soda fibers, violet; groundwood, greenish yellow; rag fibers, wine red. M. S. D.

The Bark of American Larch. K. E. Larsen and E. V. Lynn. *J. A. Ph. A. 26,* 288 (1937). The bark and other parts of the Larix americana (Muench) Michx, has been used by several of the Indian tribes as a treatment for chronic bronchitis, inflammation of the urinary passages and in phases of hemorrhage. Its use was adopted by the early white settlers who gradually added to the list of its applications. The authors obtained bark near Westminster, Mass., in the late autumn of 1934. This was air dried and ground to a No. 20 powder. Analysis of this material by the usual methods gave the following results, based on air-dried bark:

Volatile at 110 degrees C.	6.50
Ash	2.12
Acid-insoluble ash	0.22
Crude fiber	29.70
Starch, by acid hydrolysis	14.03
Pentosans	7.80
Tannins	6.49
Alcoholic extract	20.96
Diluted alcoholic extract	21.74
Successive extractions:	
Benzoin, volatile	0.22
Non-volatile	4.19
Ether, volatile	0.60
Non-volatile	5.50
Alcohol	14.65
Water	4.15

No crystalline glucoside was observed. Alkaloidal tests were negative. The ash was high in manganese.

By steam distillation, a small amount of a white aromatic solid with an odor somewhat like borneol was obtained. Tannins were of the catechol type. Saponins were indicated. About 10 per cent. of the bark consisted of a brick-red resin. M. S. DUNN.

A Rapid Method for the Determination of Triethanolamine. C. J. Eastland, N. Evers and T. F. West. *The Analyst 62,* 261 (1937). In view of the increasing number of products containing triethanolamine as a constituent, a rapid method for its determination, especially

in the presence of a large quantity of non-saponifiable substances, is desirable.

Since commercial triethanolamine may contain 20 or more per cent. of the mono- and diethanol compounds, a sample of pure triethanolamine for this work was prepared as follows: Commercial triethanolamine was neutralized to methyl orange with conc. hydrochloric acid, allowed to stand for an hour, filtered, washed and dried. The white solid was added to isopropyl alcohol to which an equivalent amount of sodium hydroxide had been added, refluxed for three hours, and after standing overnight, the precipitated sodium chloride was filtered off. The isopropyl alcohol was removed by distillation at atmospheric pressure after which the triethanolamine was distilled over at 194 to 195 degrees C. at 10 mm. pressure.

A solution of the crystals in water yielded, with Kraut's reagent (bismuth nitrate and potassium iodide in nitric acid medium) the red crystalline precipitate characteristic of triethanolamine. In the determination of this pure triethanolamine, about 0.2 gm. of the substance was dissolved in 2 ml. of hydrochloric acid (sp. gr. 1.16) and the solution evaporated to dryness, the resulting hydrochloride forming a hard skin on the bottom of the beaker. This was dried and allowed to cool in a desiccator. The crystals were then washed on to a sintered glass crucible with four portions of 5 ml. each of pure isopropyl alcohol and dried at 100 degrees C. to constant weight. A correction of 0.003 gm. to allow for the slight solubility of unrecrystallized hydrochloride in isopropyl alcohol at 20 degrees C. was added.

To extract triethanolamine from emulsions, the authors recommend mixing about 5 gm. of the cream with 20 ml. of water and heating on a water bath for five minutes. Add sulfuric acid until a blue color is given with Congo-red paper (about pH 3) and continue heating for another minute. Transfer the cooled mixture to a separatory funnel and extract the fat with two 25 ml. portions of ether. Shake the ether extracts with 20 ml. of 0.1N sulfuric acid and distil off the ether. Re-extract with ether and add the aqueous layer to that obtained from the previous extraction. Remove the sulfuric acid by precipitation with barium hydroxide. Warm and decant the supernatant liquid and remove the excess barium by passing carbon dioxide into the boiling solution. Cool, filter and concentrate. Wash into a beaker with ethyl alcohol, removing any insoluble matter by filtering. Remove the alcohol by evaporation and add to the residue

2 ml. of hydrochloric acid (sp. gr.). Determine the triethanolamine as described above.

The results obtained with emulsions containing known amounts of triethanolamine in the presence of glycerol, "sulfonated" alcohols, ammonium compounds, alkaloids, etc., were found to agree rather well with the quantities added.

In connection with this research it was found that Middleton's test for ethylene glycol in mixtures gave a positive reaction with triethanolamine because of the hydrolysis of the latter to form ethylene glycol. To test for ethylene glycol in the presence of triethanolamine the authors recommend the use of phosphotungstic acid to precipitate triethanolamine before applying Middleton's test. W. G. B.

Chlorine Therapy of Infectious Hemorrhagic Colitis. N. A. Kevdin and Shikh-Mametbekov. *Sovet. vrach. Zhurnal 1842* (1936), through *J. Am. Med. Assoc. 108,* 852 (1937). Sixty-one cases of colitis were treated with chlorine enemas. There were nine cases of amebic dysentery, eight cases caused by lambliasis, twenty-six by the bacillus of dysentery (Flexner), six by the bacillus of dysentery (Shiga), and twelve were of unknown etiology. The enemas consisted of from 600-900 cc. of chlorine water (1:50,000). The chronic amebic cases were not benefited by this therapy, but rapid improvement was noted in thirty-nine of the acute cases. The effect was probably due to a bactericidal action of the chlorine ions and the liberated oxygen. Further study is needed to definitely determine the mode of action of the chlorine. L. G.

The Relationship Between Oral and Gastric Bacterial Flora. M. Hood and L. Arnold. *Am. J. Digestic Diseases Nutrition 4,* 40 (1937). The bacterial flora from the oral cavities and gastric contents of twenty-five patients as shown by cultures revealed a close similarity. Test organisms disappeared from the mouth within two hours and thirty-six minutes after seeding. The disappearance rate from the stomach was one hour and eighteen minutes. Normal saline as a mouth wash was as effective as some antiseptic mouth washes in reducing bacterial flora of the mouth and the stomach. The reduction in the bacterial content was in all probability due to the mechanical action of rinsing the mouth. L. G.

THE TUBERCULIN TEST

By Louis Gershenfeld, Ph. M., B. Sc., P. D.

Significance of the Tuberculin Test. F. E. Harrington, J. A. Myers and N. M. Levine. *J. A. M. A. 108,* 1309 (1937). The incidence of positive reactors to tuberculin among the children and young adults is the best criterion of the tuberculosis problem in any community. It is far superior to mortality rates, since many persons who have tuberculosis die of other causes and the death certificates do not record the coexisting tuberculosis. One has only to consult postmortem records to obtain abundant evidence of this fact. Moreover, the morbidity rate does not approach the accuracy of the tuberculin test as a criterion of the tuberculosis problem, since, in approximately 80 per cent. of patients, symptoms are a late manifestation and do not bring patients to physicians for diagnosis until the disease is well advanced. Indeed, there is an average period of approximately two and one-half years before symptoms appear during which the disease can be located by modern methods. In most cases there is a much longer period after the tuberculin test is positive before there is any evidence of disease on the X-ray film.

The tuberculin test is extremely valuable in determining who in a family or in a community has foci of tubercle bacilli in the body. A positive reaction is diagnostic of the first infection type (primary complex) somewhere in the body. This type rarely causes significant illness but is always the forerunner of reinfection destructive forms of disease, both acute and chronic, when this type develops. The tuberculin test, therefore, serves as a screen to select those who have been infected through direct or indirect exposure and who should be carefully examined and kept under close observation thereafter for the development of clinical disease.

Some workers have found more positive reactions with Old Tuberculin, while others have reported more with Purified Protein Derivative. The recent work of Plunkett showed that when the larger doses of the two preparations are employed simultaneously at different sites on the same individuals there is essentially no difference in the percentage of positive reactors. The potency of Old Tuberculin from various drug houses varies considerably. This is a rather serious objection. The chief advantage of Purified Protein Derivative is that it is standardized, so that its potency is the same wherever it is

used. This, of course, insures more uniform results than when Old Tuberculin is used. The only objection to Purified Protein Derivative is its high cost.

Some physicians prefer other methods of administration than the intracutaneous, and also some persons object to the use of a hypodermic needle. For example, Chadwick, Pope and their co-workers use the epidermal method of Pirquet with excellent results. Slater, by carefully administering tuberculin by the epidermal method on one arm and by the intracutaneous method of Mantoux on the other arm, finds a difference in positive reactions of only 1 per cent. in favor of the intracutaneous method. However, in the hands of less experienced workers a larger discrepancy is usually reported. For those who even object to the scarification of the skin necessary for the epidermal test, a modification of the percutaneous test described by Lovett and the tape test by Wolff are valuable. Indeed these tests, when carefully administered, closely approximate in accuracy the intracutaneous test. However, their administration is slightly more time consuming.

The tuberculin test is no less specific for human beings than it is for cattle. Indeed, the veterinarian uses tuberculin made from the human type of tubercle bacilli for testing cattle just as we do for testing human beings.

We know all that is necessary in order to control tuberculosis in the human family, and the method now in use has been proved to be sound. If this method is employed everywhere no immunizing agent will be needed. In fact, to the present time no satisfactory immunizing agent has been developed. The veterinarians have made numerous attempts to immunize cattle against tuberculosis. As early as 1913, Moore said: "It is impossible in a work of this kind to enter into a discussion of the theories of immunity, but the fact that individuals who have suffered an attack of tuberculosis and have recovered at least temporarily are not protected against a subsequent attack or recurrence does not argue in favor of a protective vaccination. Success may be attained but at present there seems to be no method that can be recommended to the cattle owner for successfully vaccinating or immunizing his animals against tuberculosis."

Since Moore's statement, other attempts have been made, including such preparations as Calmette's vaccine, BCG. After sufficient trial, however, the veterinarians of America have not adopted BCG

as a satisfactory method of prevention. They have had a better opportunity to observe the effects of BCG on cattle than we could ever hope to have on human beings. The veterinarian's experience and his record of success in controlling tuberculosis, which is the best of any group of workers of any time, should discourage every physician from administering BCG to children. Certainly a preparation that the veterinarian considers unsafe and ineffective for cattle should not be used in an experimental way on the children of the United States. To prove the efficaciousness of an immunizing agent for tuberculosis in the human body would require decades; in fact, before this can be proved, our present method should reduce the disease in the human family to one of minor importance.

. . .

The Present Status of the Tuberculin Test. H. L. Fuerstman. *Arch. Pediat. 53,* 810 (1936). Routine tuberculin testing of children is suggested as a public health measure. Positive reactors should receive well directed home care, and a periodic medical follow-up. Negative reactors should be retested annually. The presence of a negative reaction is of importance in contact children selected for the Calmette method of prophylactic immunization with BCG vaccine.

. . .

Practical Aspects in the Diagnostic Use of Tuberculin. W. E. Nelson. *Ohio State M. J. 33,* 283 (1937). The purified protein derivative (P. P. D.) is the tuberculin of choice. The intracutaneous test is the most sensitive and reliable of the tuberculin tests. No evidence of an active disease process is given by a positive reaction, the latter being considered as an edema and erythema of five or more millimeters which persists for forty-eight hours or longer. A false negative may be given in certain acute diseases.

Therapeutics of Maggot Active Principle. Clinical Application in 1020 Cases. S. K. Livingston. *Am. J. Surg.* 35, 554 (1937). Four hundred and fifteen cases of wounds were treated by living maggots and maggot active principle and 605 cases were treated with the latter alone. Clinical improvement was noted in from 60-100 per cent. of the cases treated. Growth stimulation and an inhibition of the pathogenic bacteria resulted. L. G.

New Antitoxin Promises a Cure of Gonorrhea. Science News Letter, April 17, 1937. A new antitoxin which promises to be a specific cure for gonorrhea, was reported by Dr. T. Anwyl-Davies of St. Thomas' Hospital, London, at the conference of state and provincial health authorities of North America meeting at the United States Public Health Service.

The new antitoxin is still in the experimental stage but Dr. Anwyl-Davies' results with it seem so encouraging that it will be tried by the United States Public Health Service at its venereal disease clinic at the United States Marine Hospital, Stapleton, N. Y., Dr. R. A. Vonderlehr, of the federal health service, said.

Dr. Anwyl-Davies reported excellent results in about half the 157 cases treated with this antitoxin and good results in another quarter of the cases. "Cures" were effected in thirty-six cases which have been observed for over three months. Two of these were cured in sixteen days while other cases took up to eight weeks.

The antitoxin is equally effective in acute and chronic cases, with and without complications, the British physician reported. It differs from other antitoxins previously tried in this disease in the way it is prepared. Instead of being made by injecting the germ of the disease, the gonococcus, directly into horses, the toxin or poison produced by the gonococcus is injected into horses and the serum of these animals used as the antitoxin.

Better Pneumonia Serum Obtained From Rabbits (New Weapon Against the Pneumococcus More Effective Because Antibody Molecules Smaller; Is Also Cheaper). *Science News Letter,* April 17, 1937. A new and better way of making serum to cure pneumonia was described by Dr. Rufus Cole, of the hospital of the Rockefeller Institute, New York City, at the Conference of State and Provincial Health Authorities of North America.

Using rabbits instead of horses, two associates of Dr. Cole, Drs. Kenneth Goodner and Frank I. Horsfall, were able to make a serum that is more effective and cheaper to produce. Greater effectiveness results from the fact that the antibody molecules produced in the rabbit's body to fight the pneumonia germs are smaller than the horse's antibodies and consequently spread more rapidly through tissues infected with pneumonia germs. Fighting pneumonia due to the pneumococcus depends on getting as many of these fighting antibodies into the patient's body as possible. The patient produces some himself, but the serum gives him a big extra force. For this reason Dr. Cole advocates large doses of serum, given as early in the disease as possible. L. G.

Antipneumococcus Rabbit Serum as a Therapeutic Agent in Lobar Pneumonia. F. L. Horsfall, K. Goodner, C. M. MacLeod and A. H. Harris, 2d. *J. A. M. A. 108,* 1483 (1937). Twenty-two patients were treated with unconcentrated type specific rabbit antipneumococcus serums. From the results it appears that the latter are at least as effective as concentrated horse serum in the treatment of lobar pneumonia. This fact when added to the relative rapidity and ease with which it can be produced, the relatively low cost of the finished product, the facility with which it can be administered, as well as the evidence indicating that rabbit antibody can penetrate the pleura and assist in the sterilization of an infected exudate would suggest that type specific antipneumococcus rabbit serum is a therapeutic agent of considerable promise. L. G.

Poisons Found in Blood Following Extensive Burns. Science News Letter, April 17, 1937. The general intoxication or poisoning which follows an extensive burn and may result in shock and death is actually due to toxin in the blood, it appears from studies reported by Dr. Sol Roy Rosenthal, of Chicago, at the meeting of the American Association of Immunologists.

The poisonous substance, or toxin, was found in the blood after severe burns and an antitoxin which neutralized this substance was found in the blood after recovery from the burns. The poisonous substance makes the walls of small blood vessels more permeable so that blood plasma may leak through and the blood flow through these small vessels is retarded. L. G.

MANDELIC ACID—BACTERICIDAL ACTION

By Louis Gershenfeld, Ph. M., B. Sc., P. D.

Further Studies on the Use of Mandelic Acid for Infections of the Urinary Tract. E. N. Cook. *Proceedings of Staff Meetings of the Mayo Clinic 12,* 215 (1937). Mandelic acid is an aromatic, hydroxy acid which chemically is known as hydroxyphenyl acetic acid. Its use in infections of the urinary tract came as a direct outgrowth of the excellent results obtained in treating such infections by careful administration of the ketogenic diet.

Betahydroxybutyric acid was proved to be the bactericidal factor of ketonurine along with a low pH of the urine. The oral administration of this acid as a urinary antiseptic was not possible and Rosenheim, in search for a similar acid which would escape conjugation in the body, and be excreted in the urine unaltered, came on mandelic acid. He found this drug would exert a definite bactericidal effect on the urine when given in sufficient dosage providing the urine was highly acid.

Early, the drug was given in a 10 per cent. aqueous solution buffered to a pH of 6.5 to 7 by the addition of sodium bicarbonate to make it more palatable. The dose was one ounce (30 cc.) of the solution (3 gm. of the acid) four times a day. With the advent of the newer preparations of the drug, the original daily dosage of 12 gm. of the acid must be maintained and regulated according to the concentration of the solutions used.

The most satisfactory results have been obtained by administering the drug in the prescribed dosage for a period of six to twelve days. If the urine is not free of bacilli at the end of this period, experience has shown that it is better to discontinue administration of the drug for ten to fourteen days, and then institute a second course of treatment. This is done for two reasons: first, the organisms seem to build up a tolerance to the drug after a certain length of time; second, the factor of renal irritation by the drug is not definitely known as yet and such irritation must be guarded against.

Two points are essential in the satisfactory management of patients undergoing this form of therapy. The amount of fluid ingested in twenty-four hours must be limited to 1200 cc. or less, and every effort must be carried out to maintain a pH of 5.5 or below. With the newer preparations of ammonium mandelate, the urine will

maintain the desired level of pH without the use of secondary acidifying means such as ammonium nitrate or chloride, nitrohydrochloric or hydrochloric acid, and the ketogenic diet. However, in a fair percentage of cases these secondary acidifiers are required, and the combination of the above methods will produce urine of sufficiently high acidity in the largest percentage of cases. A small group of cases still remains in which it is impossible at the time to produce a urinary acidity of sufficient degree to obtain the desired bacteriostatic and bactericidal action.

Report on Mandelic Acid, for the Council on Pharmacy and Chemistry. William F. Braasch. *J. A. M. A. 108,* 1033 (1937). It has been common experience that mandelic acid will eliminate bacillary infection in a high percentage of uncomplicated cases. Considerable experience has brought out the following data: 1. Mandelic therapy will be found bactericidal in fully 80 per cent. of cases of uncomplicated urinary infection. 2. Organisms which have responded to the treatment include Escherichia coli, Aerobacter aerogenes and, in addition, members of the genera proteus, pseudomonas, alcaligenes, salmonella and shigella. Helmholz and Osterberg found that Aerobacter aerogenes and pseudomonas were more resistant than the other bacilli. Cocci are usually affected to a lesser degree by the administration of mandelic acid to adults. Helmholz, however, reported that it is efficacious when administered to some children. Streptococcus faecalis will, however, respond almost as well as bacilli. In some cases elimination of cocci has been accomplished by mandelic therapy following several intravenous injections of neoarsphenamine, or vice versa. 3. Cases frequently are observed in which mandelic therapy will produce considerable reduction in the degree of infection and improvement in symptoms, even though the bacteria are not completely eliminated from the urine. 4. As a preliminary to instrumentation or surgical treatment of the urinary tract, the drug is frequently of value even though the elimination of the infection is not accomplished.

When the proper precautions are observed, the urine usually becomes bactericidal in the course of two or three days, and bacterial elimination usually occurs within six or seven days. It is seldom necessary to continue the therapy longer than from twelve to fourteen days. In fact, it is inadvisable to continue administration of the drug

longer than this because of the possibility of renal irritation. It has been claimed that the infection very frequently recurs following a temporary elimination of bacilli. In such cases it would be advisable to repeat the mandelic therapy at intervals of a week or two. The dosage for adults is 12 gm. of mandelic acid administered daily. It is usually given in four divided doses during the day, before or after meals and at bedtime.

Failure of bacillary elimination may be attributable to any of the following complications: (1) chronic pyelonephritis of long standing, with advanced cicatricial changes in the renal pelvis, calices and ureter; (2) residual urine in any portion of the urinary tract; in many of these cases, however, the reduction in the degree of infection is frequently remarkable; (3) chronic prostatitis which reinfects the prostatic urethra and bladder; (4) lithiasis or tumor in any portion of the urinary tract; (5) foreign bodies, such as tubes, catheters, drains, incrustations or remnants of tissue, in the urinary tract, and (6) the occasional impossibility of lowering the pH to 5.5 by any known means. The following clinical symptoms are sometimes noted as the result of mandelic therapy: nausea, diarrhea, renal irritation and hematuria.

It would appear that the oral administration of mandelic acid is followed by elimination of bacillary infection in the urinary tract in a large percentage of uncomplicated cases. There is no clinical evidence to indicate that it is a severe renal irritant in the presence of a normal renal function, provided it is not continued longer than two weeks. Its use is contraindicated when there is evidence of renal insufficiency because of the possibility of causing renal irritation and since it is usually not excreted in sufficient concentration to be bactericidal.

Mandelic Acid Treatment of Urinary Tract Infection. L. R. Prins. *Minnesota Med. 20,* 167 (1937). Mandelic acid was employed in a 10 per cent. solution of ammonium mandelate or Rosenheim's formula was used: 48 grams mandelic acid, 25.6 grams $NaHCO_3$, 60 cc. lemon syrup, sufficient water to make 480 cc. with directions to take one ounce four times daily with 4 to 8 grams of ammonium chloride. The latter mixture seemed better tolerated than ammonium mandelate. Mandelic acid is the most effective orally administered urinary antiseptic thus far presented. It is not effective

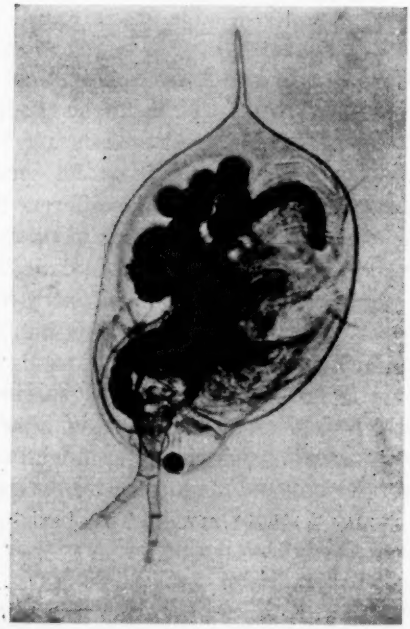
in calculus pyelonephritis, acute gonorrheal urethritis, or in the infection and pyuria following transurethral resection. It cannot be employed as a substitute when surgery is indicated.

Efficiency of State and Local Laboratories in the Performance of Serodiagnostic Tests for Syphilis. U. S. Public Health Service, Committee on Evaluation of Serodiagnostic Tests for Syphilis, *Am. J. Pub. Health 27,* 15 (1937). Sensitivities and specificities varying from 91 to 100 per cent. were obtained in different laboratories with the following diagnostic tests for syphilis: Flocculation tests—Eagle, Hinton, Johns, Kahn presumptive, Kahn standard, Kline diagnostic, Kline exclusion, micro-Hinton and modified micro-Rosenthal. Complement fixation tests—Kolmer, Bellevue Hospital, Eagle and New York State. The Meinicke clarification test was also employed. An efficient serodiagnostic test should possess a specificity of 100 per cent., and a test which yields even 1 per cent. of false positives should be so modified as to increase its specificity even with some slight sacrifice of sensitivity. A serologic diagnosis unsupported by history or clinical evidence should never be made on the basis of only one positive finding. L. G.

Ide's New Coloring Test for Syphilis. M. J. Quisumbing, *Philippine Islands M. A. 16,* 609 (1936); through *J. Am. Med. Assoc. 108,* 428 (1937). Fresh or dried blood, spinal fluid or exudate from the vesicles may be used in the Ide test for syphilis. A drop, e. g. 0.03 cc., of blood is placed on the concave surface of a hollow slide, mixed with a drop of 3.5 per cent. saline and a drop of the Ide antigen. This mixture is shaken on the slide for three or four minutes and examined under a microscope. A positive reaction is shown by the appearance of purplish blue clumps among the red cells. If the reaction is negative, only red corpuscles can be seen. If the reaction is strongly positive, the naked eye may be used. Of 119 cases giving strongly positive Wassermann reactions, 116 gave a strong Ide reaction. Of 17 cases giving weak or doubtfully positive Wassermann reactions, 6 gave weak or doubtfully positive Ide reactions. In 1126 cases showing negative Wassermann reactions, no positive Ide reactions were obtained. L. G.

CARDINAL POINTS IN FAVOR OF DAPHNIA

By Arno Viehoever*



Daphnia, showing summer eggs in the brood chamber, and the food canal, conspicuous as a black, curved tube. Mag. 18 diameters.

During the last ten years the author has in numerous publications and lectures suggested and demonstrated the use of daphnia (magna) as a biological reagent.

In the last publication † he recorded the effects of medicinal substances on the muscular, nervous and glandular systems of the daphnia, as well as on the blood and metabolism.

The interest aroused in this transparent animal for laboratory experiments, justifies, we feel, a further formulation of the various reasons why daphnia is such a satisfactory test animal.

* From the Laboratory for Biological and Biochemical Research, supported by Mr. William H. Gross, Philadelphia College of Pharmacy and Science.

† Viehoever, A.: Daphnia—The Biological Reagent, *J. Amer. Pharm. Assoc.*, 25:1112 (1936).

Cardinal Points

1. *Transparency of Body:* Presenting an intimate panorama of internal life and the unrestricted visibility of the life mechanism.

2. *Micro-Size:* Permitting close observation, optically magnified at will, of the entire animal or its organs.

3. *Complexity of Organization:* Showing differentiation in muscular, nervous and glandular systems, so essential in the organization of the human body. The evidence breaks down the physiological barrier between the invertebrate or lower—and vertebrate or higher animals.

4. *Behavior of Cold Blooded Creatures:* Demonstrating response to varied influences, reducing the importance of differences between warm and cold blooded animals.

5. *Nature of Water Animals:* Quickly and specifically reacting to stimuli, minimizing differences between water and land animals.‡

6. *Classification as Crustacean:* Placing daphnia in the scale of animal life, not included in the protective care of vivisectionists.

7. *Short Life Cycle:* Totaling approximately ninety days, comparable to ninety years of human life, permitting unlimited breeding in pure lines for genetical and biometrical studies.

8. *Quick Maturity:* Assuring development from egg to egg-bearing (up to fifty in some animals), completed within ten days and yielding great numbers of uniform animals for comparative tests.

9. *Reagent for Effect of Environment:* Permitting the study of influences, as temperature, oxygen pressure, light and other biophysical factors.

10. *Reagent for Metabolic Processes:* Showing the effect of biochemical factors, as food elements, minerals, vitamins, hormones, enzymes, etc.

11. *Reagent for Medical Agents and Poisons:* Permitting the study (exploratory and pioneering), qualitative and quantitative evaluation and standardization of drug action; stimulants, depressants, the intricate observation of therapeutic, toxic, critical and fatal doses, and the development of suitable counteragents, the check-up on synergistic or antagonistic and physiologically incompatible substances.

‡ The disturbing factor of humidity, influencing markedly the dosage of medication in human and animal experimentation, is of course altogether eliminated.

12. *Reagent for Diseases:* Disclosing pollution and suggesting possibilities in an unexplored field, e. g., bacteria and toxins.

13. *Reagent for Teaching Biology:* Assuring distinct visibility of life functions for demonstration.

14. *Reagent for Teaching Pharmacology or Materia Medica:* Replacing faith, hearsay or often *obscure* evidence by the actual demonstration of cause and effect.

15. *Economical Reagent:* Permitting experimentation and demonstration with minimum expense for feeding, breeding and care.

Many of these considerations, favoring daphnia as a living reagent, apply also to palaemonetes, a transparent prawn, found in freshwater pools.

Preventive Inoculations. D. O'Hara, *New Engl. J. Med. 216,* 236 (1937). Immunization is discussed. Vaccination under the age of one year with revaccination in early adult life are recommended as preventive measures against smallpox. Toxoid should be given between the ages of six months and one year as a prophylactic against diphtheria. Above the ages of six years, in order to avoid severe reactions toxoid should be used only after testing for sensitivity. Injections of scarlet fever toxin are recommended. The use of typhoid vaccine is confined mostly to those in military service and to persons travelling in foreign countries. Vaccines can produce some resistance to many of the secondary invaders found during "colds". Further controlled tests are needed to determine the value of convalescent serum, normal adult serum and placental extract in cases of measles. The author believes that whooping cough vaccine has no significant effect on the attack rate in inoculated children.

The Diagnosis of Whooping Cough. The Complement-fixation and Intradermal Tests. J. P. J. Paton, *Lancet 232,* 132 (1937). The complement fixation test is of value in confirming the clinical diagnosis of whooping-cough. There is evidence that the complement-fixation test becomes positive early in the infection in a high proportion of cases. Negative results were most commonly observed in very young children in whom there seems to be a poor antibody response. Other apparent causes of a negative reaction were short duration of the disease, very severe infection or presence of complications, and anti-complementary sera. The intradermal test failed to give specific re-

sults. A high percentage of patients with whooping cough gave positive reactions but so also did a group of control patients with no history of whooping cough. There was no correlation between the intradermal test and the complement-fixation reaction.

Intradermal Tests for Susceptibility to Whooping Cough. B. O'Brien, *Lancet 232,* 131 (1937). A series of 371 cases was examined for susceptibility to whooping cough by an intradermal test using Sauer's vaccine as an antigen. The results support the view that the test is, within limits, a reliable index of susceptibility to H. pertussis infections.

Intradermal Tests in Whooping Cough. J. S. Westwater, *Lancet 232,* 289 (1937).

The Treatment of Whooping Cough. John A. Toomey, *Ohio State M. J. 33,* 161 (1937). No alleviation of whooping cough in human subjects was produced by Krueger's undenatured endoantigen; by the old-fashioned vaccine in use before Sauer's vaccine; and by Sauer's vaccine prepared freshly. Pertussis mucoid exudate appeared to shorten the course of infection in eighty cases under three years of age. Inconclusive results were reported by the use of convalescent serum, employed in severely affected cases.

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* The Present Position of the Chemistry of Nutrition

Dr. Sherman in opening outlined the contributions of many earlier workers in the field of nutrition. He then described several experiments and their results as obtained in his laboratory, illustrating the trend of modern nutritional research. Although commonly known as vitamins, this group of essential food factors are now known to belong to widely different classes of chemical compounds. Their only common property is the production of various symptoms of deficiency in animals which are deprived of an adequate supply of any one vitamin.

Animal experimentation has been quite highly perfected and quantitative work given greater significance due to careful selection,

*Abstract of an address given before the Philadelphia Section of the American Chemical Society by Dr. H. C. Sherman, at the Franklin Institute, on March 18, 1937.

standardization, and breeding together with maintenance under rigidly controlled conditions.

Recent experiments have shown that, insofar as certain food factors are concerned, simply providing an adequate supply is not as beneficial to the animal as the consumption of amounts quite in excess of this level. Thus enriching the diet with certain foods supplying definite accessory food factors beyond actually required amounts was found to produce significant differences in the amount and rate of growth, the life span, fertility, per cent. of young reared and, most interesting of all, the period of adult life was increased. In one set of experiments standardized rates on simply an adequate diet had an average life span, in the case of males, of 571 days and females 603 days. Increasing the intake of these food factors increased the average life spans to 635 and 669 days respectively, with deviations of $\pm$ 11.7 and $\pm$ 11.2. This increase is of considerable significance and of sufficient magnitude to make it important from the statistical standpoint.

Dr. Sherman classified certain everyday foods as "protective foods" which he considered to be of sufficient value to the animal economy to warrant their comprising 50 per cent. of the diet. They are milk, eggs, butter, green vegetables and fruits. If this plan is followed the nature of the other 50 per cent. is of little consequence since the individual is guaranteed a food intake of proper qualifications for his growth, development and health. L. F. TICE.

The Detection and Determination of Parahydroxybenzoic Acid and Its Derivatives With Special Reference to Their Distinction From Salicylic and Benzoic Acids. F. W. Edwards, H. R. Nanji, M. K. Hassan, *Analyst 62,* 178 (1937). The use of parahydroxybenzoic acid esters as preservatives in foods and drugs is quite well known. Consequently, a method of detection and determination of these esters alone or combined with salicylic or benzoic acid becomes important. The method developed depends upon first extracting the mixed preservatives by means of an organic solvent such as alcohol or ether, hydrolyzing them with alcoholic potash, and isolating the acids as their ammonium salts in neutral solution.

A series of tests is now applied to small portions of this solution enabling one to detect benzoic, salicylic, or para-acid singly or in admixture.

I. *Millon's Test*—20 cc. of solution is treated with 2 cc. Millon's Reagent and the mixture heated on a boiling water bath for two minutes. A red color is obtained with both salicylic and para-acid, while benzoic acid gives no color. The colors obtained with the two acids when compared side by side are quite distinct, that with the para-acid being rose red and that with salicylic being orange red. However, one should not rely on these differences. Confirmatory tests are advisable, since many other phenolic substances give a color.

II. *Ferric Chloride Test*—To the solution add 1 cc. of ferric chloride solution (0.1 gm. $FeCl_3$, 20 cc. $N/_1HCl$ q. s. water to 100 cc.). Unless very large amounts of para-acid are present only salicylic produces a violet color.

III. *Jorissen's Test*—About 10-25 cc. of the solution of ammonium salt are treated with 1 cc. of 2 per cent. $NaNO_2$ and 1 cc. of 0.3 per cent. $CuSO_4.5H_2O$ in 10 per cent. acetic acid. As little as 0.1 mg. of salicylic acid gives a distinct pink color. With para-acid under the same conditions 1 mg. gives a very faint yellow. Benzoic acid gives no color. Thus this test is a good confirmatory test for salicylic and with a positive Millon followed by a negative Jorissen test the absence of salicylic and the presence of para-acid is indicated.

IV. *Copper-Salt Crystals.* This test depends upon the relative insolubility of the copper salt of para-acid which will crystallize from solution, copper salicylate being very soluble. The original article outlines the method of obtaining the crystals and presents photomicrographs showing their characteristic appearance. This test is considered important since it is the only one which will definitely prove the presence of para-acid.

V. *Nicholl's Test* (modified) and VI. *Mohler's Test* are used to establish definitely the presence or absence of benzoic acid. In the former a portion of the solution containing the ammonium salts are placed in a test tube, to it are added 5 cc. of O.1N. sulfuric acid and the volume then adjusted to 15 cc. with distilled water; 1 cc. of an iron reagent (2.7 gm. $FeCl_3$ in 13 cc. N sulfuric acid and diluted to 100 cc. with water), and 1 cc. 0.2 per cent. hydrogen peroxide are added and the whole is well mixed and heated on a boiling water bath for fifteen minutes without further shaking. The solution is then cooled and extracted with three (15 cc.) successive quantities of ether, each ethereal extract being washed with 5 cc. water. The solvent is then completely removed by distillation on a water bath at

50° C. and the residue dissolved in 50 cc. of 10 per cent. alcohol, 1 cc. of an iron solution (0.1 gm. $FeCl_3$ in 20 cc. $N/_1HCl$ and diluted to 100 cc. with water) are added and the appearance of a violet color noted which indicates benzoic acid in the sample.

VII. *Indirect Test*—The exact amount of salicylic acid in, say, 20 cc. of the neutral solution of ammonium salts is first determined by test II or III. A fresh 20 cc. portion and a standard containing this amount of salicylic acid in 20 cc. of water are taken for the Millon test. The colors obtained are compared in Nessler tubes after diluting to 50 cc.

In the absence of para-acid the two colors will match well, but if any appreciable quantity of that acid is present the tints will be different, the test solution being more rose-red than the standard.

A tabulation is presented in the original article summarizing the above tests in a schematic form. There follows individual methods for the quantitative evaluation of para-acid in various food products with the error that may be expected. L. F. T.

Culturing Staphylococcus Aureus. B. G. Philbrick, National Association Insecticide Disinfectant Manufacturers, Committee on Testing Disinfectants, meeting (Dec. 1936); through *Soap 13,* 103 (1937). Much difficulty is encountered in maintaining the standard Staphylococcus aureus culture used in the F. D. A., Phenol Coefficient technic at the prescribed resistance. As a means of controlling somewhat this marked variation, it is suggested that a standardized beef extract (Lab-Lemco) be used in the official F. D. A. broth formula.

L. G.

IODINE IN THE PREVENTION OF THYROID DISEASE

By Louis Gershenfeld, P. D., B. Sc., Ph. M.

IODINE is distributed widely though very unevenly in nature. The sea or deposits derived from the latter are responsible in the main for the supply of this element. All forms of plant and animal life living in the sea apparently contain iodine. On the other hand, iodides are present also in certain rock formations and some ores. Soils and waters from soil may contain small but usually variable amounts of iodine. Land plants may contain traces of iodine, but

this varies depending upon the iodine content of the soil in which such plants are grown.

Plants and the lower forms of animal life do not appear to possess specialized tissue for the storage and elaboration of iodine; and as yet there has been no worthwhile evidence presented to show that this element is actually required by the former. On the other hand in most all verterbrate animals and especially in all higher vertebrates including man, there is at present a specialized tissue, known as the thyroid gland, where iodine is localized and stored, later to be elaborated into a hormone.

The Thyroid and Its Iodine Content

In man the normal thyroid appears as a U-shaped gland, weighing (in adults) between 20 and 35 grams. It is composed of two lateral lobes (2 cm. by 5 to 6 cm.), connected across the midline in front of the trachea by a narrow band of thyroid tissue called the isthmus. The lobes are broad below and taper to a point above. They are attached somewhat firmly to the larynx laterally and the isthmus to the trachea, with the result that the gland moves with the trachea. Scattered along the front of the trachea as far down as the bronchi may be found small masses of thyroid tissue designated at times as accessory thyroids. The isthmus is the only portion of the thyroid gland which is readily palpable, and in practice this fact is utilized so as to detect the presence or absence of slight thyroid enlargements. It is to be noted however that in some few instances, the isthmus may be absent.

In 1895, Baumann (*Zeitschrift f. Physiolog. Chem., 21*) revealed that the thyroid gland normally contained iodine, and that this element was present here in large quantities, in reality in amounts not found in any other body tissue. He further showed that the iodine was present in organic combination and isolated a substance named by him "iodothyrin." Experimental evidence was presented which revealed that iodine was the constituent in the thyroid which was responsible for its most important function. The presence of iodine in sufficient amount was responsible for increased metabolism or heat production and its absence resulted in decreased metabolism. Various workers attempted to isolate the specific iodine-containing substance. None were successful until E. C. Kendall of the Mayo Foundation (*J. A. M. A., 54,* 2042 (1915); *71,* 871 (1918) isolated in 1916

the stable iodine-containing hormone which he called "thyroxine." Ten years later, C. R. Harington, of England (*Pharm. J., 118,* 734 (1926) prepared the latter synthetically. Researches have yielded the following valuable data: The average iodine stored in normal thyroid glands is two milligrams for each gram of dry gland. The maximum iodine storage capacity is between five or six milligrams per gram of dry gland, or a total of not more than twenty-five milligrams of iodine can be found in the normal human thyroid. This means that the maximum amount of iodine that could possibly be stored in the thyroid glands of forty normal adults would total not more than one gram. The active cells in the normal thyroid take iodine out of the circulating blood. The newly acquired iodine now present in the gland is at first inactive physiologically but it is gradually elaborated into thyroxine, the latter possessing the physiological effects of increasing the metabolic rate. It is this iodine-containing hormone, thyroxine, which is responsible for the function of the thyroid gland, in that it makes possible a higher rate of metabolism and provides the means for changing the rate of metabolism to meet varying physiologic requirements.

Diseases of The Thyroid

Disturbances arise from a decrease (hypothyroidism) or an increase (hyperthyroidism) in the activity of the gland. The important diseases associated with disturbances of thyroid function are:

1. Simple goiter, which comprises those enlargements of the thyroid gland in man and animals also designated as endemic, sporadic, epidemic, colloid, physiologic, etc. In goiter, there is a functional insufficiency of the gland. Due to this decreased functional activity of the thyroid cells, the gland reveals a compensatory enlargement.

2. Myxedema, infantile (Cretinism) and adult (Gull's disease). Occurring in early childhood, whence it is known as Cretinism, a deficiency in thyroid function produces a retardation in mental and physical growth as well as in sexual development. In adults or in later life especially in women between the ages of thirty to fifty, when the thyroid is affected to an underfunctioning degree, instead of Cretinism, there prevails a lowered metabolism, a loss of memory and expression, physical weakness and mental apathy, and one finds a thickening of the skin and an infiltration of a peculiar mucoid edema.

The latter state in which one observes a characteristic enlargement of the subcutaneous tissue is called Myxedema.

3. Graves' or Bastedo's disease (exophthalmic goiter). The prevailing thought is that Graves' disease is in reality not primarily a thyroid disease and should not be included with a consideration of primary thyroid disease. The thyroid envolvement appears to be secondary and is dependent upon some obscure deranged function of the visceral nervous system. In this condition, however, there exists a hyperthyroidism. An overactivity of the thyroid gland is revealed in a marked degree.

Iodine in Thyroid Disease

The value of iodine in the treatment of disturbances of the thyroid gland is limited. Its use is conditioned upon many factors. In fact in Graves' disease, while beneficial at times, the injurious effects of the improper use of iodine may be serious. Even in the treatment of simple goiter, endocrinologists do not limit themselves to the use of iodine alone, but this therapy is combined with the administration of desiccated whole thyroid and even other medicaments. The injurious effects of the excessive or indiscriminate use of iodine in the treatment of all kinds of thyroid disturbances are real, often serious, and were observed and described as far back as 1821 by the Geneva physician, Coindet, and in 1822 by Gairdner.

Simple Goiter and The Use of Iodine in Its Prevention

Simple goiter occurs among all races, sexes (though more frequent among females than males) and in all climates. It is observed less frequently among those living near sea coasts, and a striking characteristic is the large number of cases found in certain regions of the world known as the endemic goiter districts. These so-called "goiter belts" are found in Europe, in the region of the Alps, including Switzerland, northern Italy, northern France and the Balkan States; in the Himalaya Mountains of eastern, central and southern Asia; and in the Andes Plateau in South America. The goiter area in our own country centers about the region of the Great Lakes and the St. Lawrence River and the Cascade Mountain territory of Oregon, Washington and British Columbia. Of minor importance are regions throughout the Appalachian and Rocky Mountains and some foci throughout several states in the Central Basin. Outbreaks

of large numbers of goiter cases, so-called epidemics, have been reported. Simple goiter occurs most frequently during those periods of life when growth, energy transformation and differentiation are at their greatest as during fetal life, puberty, pregnancy and during the menopause.

A review of the history will reveal an exceedingly large number of theories which account for the cause of simple goiter. Within the past year Boissevain and Drea (*Endocrinology, 20,* 686, 1936) reported an investigation on the relation between the occurrence of endemic goiter and the presence of traces of silver and barium in drinking water. In their observations water from the goiter region in Switzerland revealed the presence of an unusually large amount of barium. Experimental feeding of rats failed to show any influence possessed by either barium or silver on the development of goiter. In the light of our present knowledge, one can say that simple goiter is caused by the lack of iodine and not necessarily due to the introduction of some agent capable of producing such abnormality. Of historical interest, one may note that Humboldt in 1824 described an endemic goiter region in Colombia, South America, and referred to the fact that the natives knew of the existence of one salt deposit which was more beneficial than any other salt in the treatment of goiter. Later Roulin and Boussingault showed that this deposit which was found useful contained the most iodine. In 1852, Chatin found that the soil and water in endemic goiter regions were low in the iodine content or that this element was even absent. Goiter Commissions were appointed by different governments during the last century for the purpose of instituting measures to prevent this affection. Various measures were recommended and practiced. It remained for Marine and Lenhart in 1910 to actually add iodine to water (in a concentration of not greater than one milligram per liter) so as to prevent or arrest the development of goiter in brook trout. The addition of iodine has successfully been used in the prevention of goiter in poultry, cattle, sheep and pigs. In 1917, Marine and Kimball were the first to introduce a method of prevention in human goiter, when they experimented for a period of over two and one-half years with a large number of girls attending the public schools in the city of Akron. Their method consisted in giving two grams of sodium iodide in 0.2 gram doses, distributing the dosage over a period of two weeks and administering this amount twice each year during the spring and autumn.

Iodized Salt

Extensive investigations were carried out by different workers on the use of iodine in the prevention of goiter. The conclusions are that the greatest value of iodine in thyroid disease is in its prevention. Simple goiter in man is preventable by the administration of a daily dose of not more than one milligram of iodine, the latter being effective when given in any form or introduced in any manner. Accordingly iodine has been given in the form of syrup of hydriodic acid, using one or two ounces, twice each year. A concentration of one part of iodine per million parts of water given for a period of two weeks each autumn and spring was also advocated. A very effective and widely recommended procedure for prophylaxis was the introduction of iodized salt. The latter was prepared by adding 0.01 per cent. sodium or potassium iodide to table salt, or ten milligrams of the former to each 100 grams of the latter. Later, in 1924, the salt manufacturers marketed an iodized salt containing one part of potassium iodide to 5000 parts of table salt. This product was advertised and used especially throughout the State of Michigan upon the recommendation of the medical profession and the health department of that state. Shortly thereafter, warnings and notes of caution were sounded as to the safety of this so-called indiscriminate use of iodine. Among the many warnings is to be found an interesting contribution by Horn (*Am. J. Pharm., 102,* 242, 1930) on "Iodized Salt—A Food or a Drug." Recently Kimball (*J. A. M. A., 108,* 860, 1937) presented a report on the program of goiter prevention in Michigan and Ohio and upon the use of iodized salt. This contribution is a valuable one and should be consulted for more complete details. The important findings to be noted are the following:

Many of the brands of iodized salt were below the required amounts of iodine and below the amounts designated on the labels. In three instances, iodine was absent though the labels of these iodized salts stated that 0.023 per cent. of potassium iodide was present.

The survey shows that the general use of a properly iodized salt is an efficient and safe method of goiter prophylaxis, and every community where *goiter is endemic* is advised to meet the deficiency of food iodine by the use of iodized salt.

SOLID EXTRACTS

By Ivor Griffith, Ph. M., Sc. D.

Despite the form in which this information is presented it may be accepted as trustworthy and up-to-date. Original sources are not listed but they may be obtained upon request.

On February 6, 1787 (five years after the peace with Britain), Dr. Benjamin Rush delivered a discourse before the venerable College of Physicians of Philadelphia. Its concluding paragraph, though written one hundred and fifty years ago, is so sound in its optimism and so serene in its spirit, that it might well have been written for today.

"I shall conclude with the following remarks. It is a general opinion that the condition of man in our world is mending. The conveniences and pleasures of life are daily multiplying by the inventions of philosophy. Many disorders, once deemed incurable, now yield to medicine. No wonder then that a general expectation prevails—that a revolution is soon to take place in favour of human happiness. Natural means appear to be the instruments designed by heaven to fulfill its purposes of mercy and benevolence to mankind. I am fully persuaded there does not exist a disease in nature, that has not an antidote to it."

College Life in Germany is now on a "Fuehrer" basis! And how strange it is to read such monstrosities and absurdities as these portions of the new regulations.

"Planned 'sings' and other musical activities, and carefully arranged social evenings may perhaps eventually come to take the place of the old student 'kommerse' (the drinking bouts that were a famous feature of German student life). A new students' code of honor has also been created, based on the absolute satisfaction of affronts by the duel. This code, still in process of being drafted, regulates dueling and the use of weapons, with particular reference to saber duels. Affairs of honor will be decided by the saber duel. Since drunkenness is considered unworthy of a German, a student who receives an affront while he is intoxicated has no right to demand satisfaction. If a Ger-

man student, while under the influence of drink, should offend the honor of a fellow student, the incident must be settled otherwise than by dueling."

For all that we know, and for all that we think we know, there remain the boundless vastnesses of the what we do not know.

Man is yet as a groping child, and millenia behind his real manhood. Of the simplest of earthly materials, *water,* we think we know much. Actually we know but little of its real character.

For instance, what do we know of the watery ectoplasm? What do we know of the communicable livingness of natural water—of its constantly changing and invigorating freightage of vital units?

Why do those armadillo-minded magisters of mysteries, the so-called scientists, deride such a statement as this: "Rain falling during an electric storm is more life giving to plants than ordinary rain. When collected in earthenware pots it holds this virtue, but if collected in iron pots it is quickly dissipated." In the old country such rain was stored in large crocks for watering flower gardens.

Is it not safe to assume that rain carries virile electric charges which in earthenware pots are insulated, but which are promptly *grounded* by iron or metal pots?

I have it on reliable authority that the odor so lacking in the American wild violet may be considerably developed if they be placed in cultivation, and grown under red glass. The concentration of the long, heating, *red rays may be responsible for such development, for it is a well established fact that odorous plants grown on sunny slopes are much more free with scent than those in more secluded, sun-excluded spots.*

"I know a bank
Whereon the wild thyme blows"

sings the poet—and any lad of the English countryside knows full well and without moralizing that the primrose path was never more glowing, never more sweetly scented than when it received, because of its exposure, the sun's benediction, from rise to set.

It is hardly believable that nearly fifty million pounds of snuff are manufactured annually in this country although snuff devotees are rarely encountered here.

The use of snuff was once so popular that Pope Urban VIII in 1624 issued an edict of excommunication against its use during church services, because snuffing and sneezing interrupted the religious ceremonies. Its use spread to England, Scotland and Ireland, and in the eighteenth century snuff taking became the fashion, the lords and ladies taking it in pinches and the scullions and cooks in handfuls. Charles IX, Napoleon, Frederick the Great, Queen Charlotte, Marie Antoinette, all the Georges of England, Lord Nelson, Count von Moltke were devotees of the powdered weed. Dryden, Pope, Swift, Sterne, Addison, Goldsmith, Coleridge, Burns, Doctor Johnson, and other literateurs, took snuff. The method of taking snuff, of opening and tapping the snuff box, became a fine art, and a gentleman was appraised according to his snuffing and sniffing technique.

No sense outsenses the nose sense. Our nose knows more than we think it knows, and awakens our memories and emotions more promptly than the rest of our senses.

The amount of an odorous substance necessary to produce the sensation of smell is incredibly minute. Camphor is said to be detected in a dilution of one part in four hundred thousand, musk one in eight million, and vanillin one in ten million. Valentin found that one twenty-thousandth of a milligram (less than a millionth of a grain) of otto of rose was all that was required. Fischer and Penzoldt determined that one 460-millionth of a milligram of the rotten egg odor of ethyl mercaptan was the approximate minimum amount which, coming into contact with the olfactory nerves, could be immediately recognized by them, which is about 250 times less than the minimum amount of sodium which can be detected by the spectroscope, according to the experiments of Kirchoff and Bunsen.

The pleasant odor of the soil was ascribed by Berthelot, the distinguished French chemist, to traces of an unidentified camphoraceous body of so powerful a fragrance that even a trillionth of a milligram gave a clearly perceptible aroma.

And speaking of knowing noses, here is a voting result of a group's likes and dislikes with certain odors: (1) rose (85 per cent.), (2) pine (83), (3) lilac (83), (4) violet (77), (5) lily-of-the-valley (77), (6) coffee (76), (7) balsam (76), (8) cedar (73), (9) straw-

berry (68), (10) wintergreen and apple (67). Those disliked, arranged similarly were: (1) perspiration (97 per cent.), (2) garlic (92), (3) rubber (81), (4) lard (79), (5) kerosene (77), (6) olive oil (70), (7) fish (70), (8) onion (66), (9) turpentine (63), (10) gasoline (59).

When fruits and vegetables are sprayed with the poisonous insecticides lead and arsenic, these are not blown or washed away but are retained by the soil to which they have fallen, "only to be gradually released and taken up by the vegetation growing on such soil," warned Dr. P. J. Hanzlik, Stanford University pharmacologist, in *The Scientific Monthly.* For the last twenty years, he said, a valley in the Pacific Northwest has received annually as much as 7,000,000 pounds of lead arsenate.

For consumers of sprayed fruits and vegetables from which the poisonous chemicals have not been entirely removed, Dr. Hanzlik held protracted ill health, even death, to be the ultimate unhappy prospect.*

"Economic losses in livestock have been so large in sprayed regions as to cause growers to give up business," he declared. "Turkeys allowed to run in sprayed apple orchards are known to have developed lead poisoning."

Until such time as insecticides not deleterious to health are developed, Dr. Hanzlik recommended that "producers should avoid the use of lead arsenate or other arsenicals on vegetables consumed in their entirety."

* Reported Chief W. R. Wharton, of the eastern district, Food and Drug Administration, to Health Officers of New Jersey: "During the last fiscal year 6,632 samples of fruits and vegetables were tested for poisonous residues with the result that 146 shipments containing residues in excess of the tolerances (i. e., amounts which can be endured with apparent impunity) were proceeded against and seized and numerous prosecutions followed. Products so seized and removed from the market included apples, crabapples, pears, currants, cherries, plums, quinces, cabbage and cauliflower."

BOOK REVIEWS

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

TEXTBOOK OF PHARMACOLOGY.

Originally prepared by Poulsson in 1909 for physicians and students, the eleventh edition has been revised by Liljestrand with 622 pages, forty-one illustrations; published in German by S. Hirzel, Leipzig, 1937. Bound. Mark 16:50.

The subject matter is discussed in seven chapters:

I. Organic substances, acting after resorption, including narcotics of the hydrocarbon series and alkaloids, glucosidal drugs, antipyrin and derivatives, as well as antiseptics of the aromatic series, e. g., phenols, benzoic acid and derivatives, and finally amino and nucleic acids.

II. Organic substances, acting locally, as mucilaginous, sweet, bitter and astringent substances; ethereal oils, skin irritants, vegetable laxatives and anthelmintics.

III. Alkalies and alkaline earths, and their salts, acids, halogens, oxidants, phosphorus and arsenic.

IV. Heavy metals.

V. Ferments and nutrients (protein preparations and carbohydrates).

VI. Hormones and vitamines.

VII. (Antitoxin and bacteria products—especially sera).

As Poulsson was experimentally active in the field of pharmacology and an efficient contributor to Heffter's handbook of experimental pharmacology, the textbook, fortunately, reflects this personal experience.

While one may question the wisdom of the interesting but rather loose grouping of physiologically active substances, particularly evident in the first three chapters, the treatment of the individual monographs is exemplary. The discussion of the chemistry is usually followed by that of the effects, therapeutic application, preparations and dosage.

Although the book, in common with other textbooks, is conservative and restricted to accepted facts, one may well wish the author the opportunity of frequent revisions, so that the latest achievements such as the isolation of the physiologically active phtioic acid from tubercle bacilli and other important findings, in such an awakened field of medical science as pharmacology, may more quickly come to the attention of student, practitioner or laboratory worker.

The book is a credit to the authors for its clarity and scope of treatment; to the publishers for the excellency in the printing arts.

A. VIEHOEVER.

Editorial note: Through the courtesy of the reviewer and of *The Chemist,* publication of the American Institute of Chemists, we are privileged to reprint these two really revealing reviews.

MORE FOR YOUR MONEY. H. Bennett, F. A. I. C. Chemical Publishing Company of New York, Inc., 1937. xii + 251 pp. Price, $2.75.

THE COSMETIC FORMULARY. H. Bennett, F. A. I. C. Chemical Publishing Company of New York, Inc., 1937. xix + 259 pp. Price, $3.75.

Although it is not uncommon nowadays for a reviewer to be given several books on the same or related subjects, by different authors, published within a short time, it is a rare privilege to have in hand two quite different books by the same author, printed in different countries and published almost simultaneously.

In *More for Your Money,* the protean Mr. Bennett is lined up with the professional reformers—but with a commendable difference of intent. Instead of being merely destructive of everything we like to buy for our beauty, health and happiness, he strives to warn us against the most flagrant deceptions, and show us how to protect ourselves by making tests on everything and sundry.

The introductory chapters on buying in general, and how to read labels and check quantities, contain much good information for consumers. The rest of the book discusses cosmetics and drugs; foods and beverages; electrical devices and other household equipment and furnishings; all kinds of clothing; jewelry and optical goods; building materials, automobiles, mail order courses in this and that, and still more "miscellaneous" items. Most of the material is acknowledged to have been lifted from various government publications and from the "Better Buymanship" pamphlets of the Household Finance Corporation, Chicago, and the debt is disconcertingly obvious in the frequent changes in the literary style.

Multiplicity of sources also multiplies a compiler's chances for a good "alibi". When, for instance, the reader is told (page 20) that to test for lead in a hair dye, he should put some of the suspected colorless solution into a beaker, add some HCl, and look for a black precipitate of PbS, one is tempted to ask, "What kind of chemistry—whose private brand of chemistry—is that?" Other errors, inaccuracies, wrong deductions and misleading inferences range from merely silly to potentially dangerous.

A chemist or teacher, who wants to save the trouble of assembling information from all the same sources, might find this book useful as

a skeleton guide for consumer education. Such a trained person would undoubtedly have other knowledge to substitute for what is not usable here, but the poor consumers for whom this work is intended could do little for themselves. Unless they know their way about in a well-stocked chemical laboratory, this book would be but a bewildering and expensive guide to safety.

From the "worm's-eye view" of the cosmetic industry, so readily acquired from the one superficial chapter in *More for Your Money,* any uninitiated reader would be dazzled by the brilliant possibilities set forth in *The Cosmetic Formulary.* Here are thousands of recipes for everything made in the cosmetic and allied industries. With unseemly avidity, one notes that many of the substances mentioned fearsomely in the other book are suggested here for use in depilatories, dyes, deodorants, etc.

The first book preaches the publication of formulas on labels so that the poor benighted public will know what is being perpetrated on it; but what earthly good (besides publicity) can be derived from publishing synthetic names of unexplained proprietary ingredients? The text is followed by useful conversion tables, common names of chemicals, and lists of manufacturers of raw materials and equipment. Tracing a proprietary name through these lists to a source makes a nice little game.

Reviewing two such books together arouses a welter of conflicting thought. There is a definite place for any good, carefully edited formulary, but it should serve as a means, not as an end in itself.

Following in the wake of too many books which convey the idea that "anyone can be a chemist," this one furthers another fallacy—that "anyone can make cosmetics." It seems not to have occurred to our colleague that it is just "patient experimenting" out of books like this which gives "fly-by-nighters" the chance to concoct messes in shadowy back rooms, peddle them at cut rates, and thus cause unfair competition and much exasperation to legitimate manufacturers who spend good time and money in research and testing before they release their products to the consumer. The professional crusaders, recommended so highly in the other book, raise so much dust belaboring the more obvious camels that they usually do not see these troublesome gnats.

One more inconsistency here: after a comprehensive summary of manufacturing procedures, the "experimenter" is told, in effect, that as a last resort—when he becomes hopelessly stuck—he should call on a consulting chemist. Oh, it is all very sad, and *very* confusing!

FLORENCE E. WALL, F. A. I. C.